SEARCH REQUEST FORM

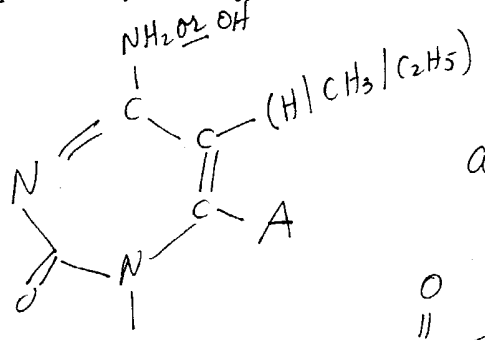
Requestor's Name: BERCH Serial Number: 10/663414

Date: 7/14/04 Phone: 571-272-0663 Art Unit: 1624

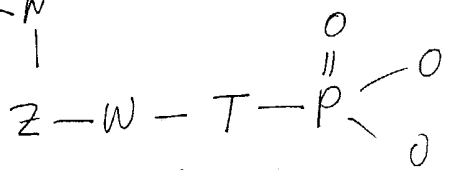
Office Rem 5C01 Mailbox 5C18

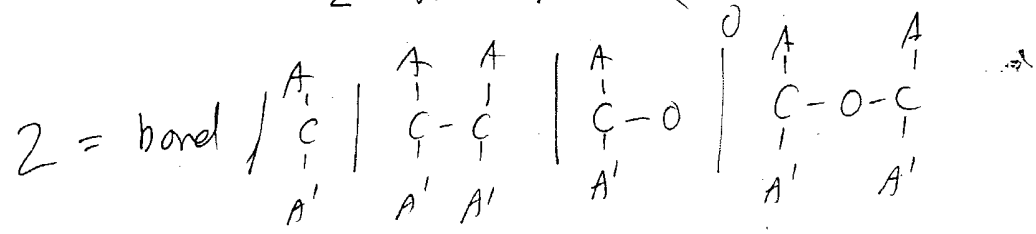
Search Topic:

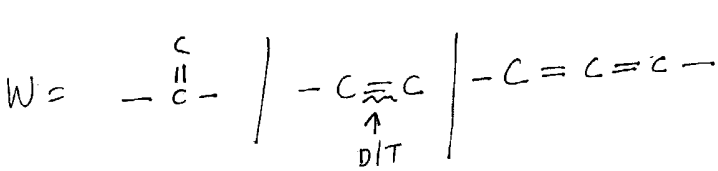
Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevent citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevent claim(s).



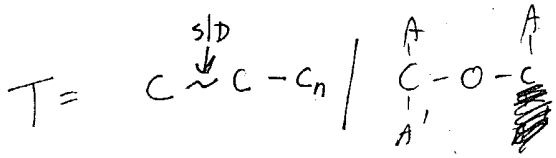
all A = H/CH3







all carbons depicted in W and T must be in chain



n = 0-1

STAFF USE ONLY

Date completed: 7/20/04

Searcher: P. Reppert

Terminal time:

Elapsed time:

CPU time:

Total time: 2h

Number of Searches:

Number of Databases: 2

Search Site

- ✓ STIC
- CM-1
- Pre-S

Type of Search

- N.A. Sequence
- A.A. Sequence
- Structure
- Bibliographic

Vendors

- IG
- ✓ STN
- Dialog
- APS
- Geninfo
- SDC
- DARC/Questel
- Other

```
=> b hcaplus
FILE 'HCAPLUS' ENTERED AT 16:19:04 ON 20 JUL 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 20 Jul 2004  VOL 141 ISS 4
FILE LAST UPDATED: 19 Jul 2004  (20040719/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que l71
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L69               STR
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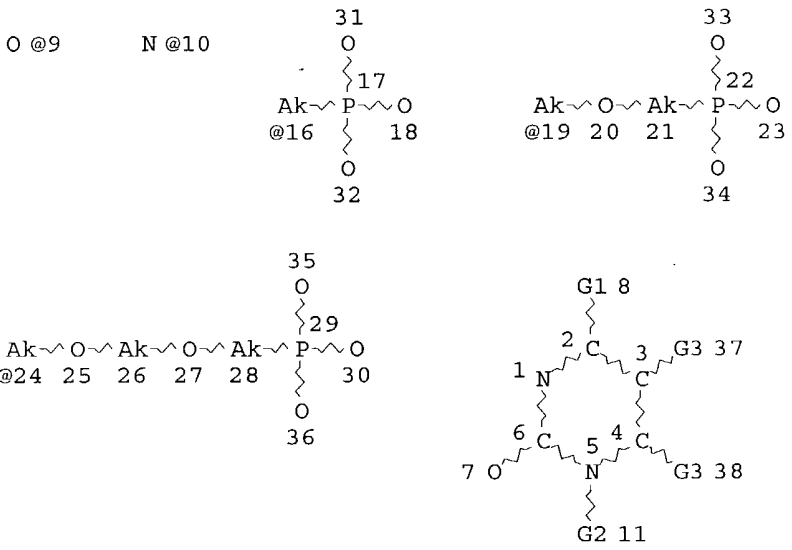


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VAR G2=16/19/24
VAR G3=H/AK
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CONNECT IS M1  RC AT  36
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  34

STEREO ATTRIBUTES: NONE
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L71           45 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L70


=> d ibib abs hitstr l71

L71  ANSWER 1 OF 45  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2003:922664  HCAPLUS
DOCUMENT NUMBER:          140:5264
TITLE:                    preparation of anti-retroviral enantiomeric nucleotide
                          analogs
INVENTOR(S):              Holy, Antonin; Dvorakova, Hana; De Clercq, Erik Desire
                          Alice; Balzarini, Jan Marie Rene
PATENT ASSIGNEE(S):       Institute of Organic Chemistry and Biochemistry, Czech
                          Rep.; Rega Stichting V.Z.W.
SOURCE:                   U.S., 24 pp., Cont.-in-part of U.S. 6,057,305.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
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     US 6653296         B1   20031125       US 1995-379551   19950202
     US 6057305         A    20000502       US 1992-925610   19920805
     WO 9403467         A2   19940217       WO 1993-US7360   19930804
     WO 9403467         A3   19940623
         W:  CA, CZ, JP, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     EP 897917          A1   19990224         EP 1998-119443   19930804
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE
     JP 2004189750      A2   20040708         JP 2004-29994    20040205
PRIORITY APPLN. INFO.:                    US 1992-925610   A2 19920805
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OTHER SOURCE(S):          MARPAT 140:5264
GI
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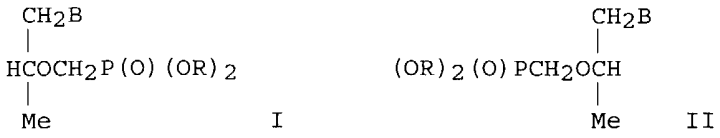


I II

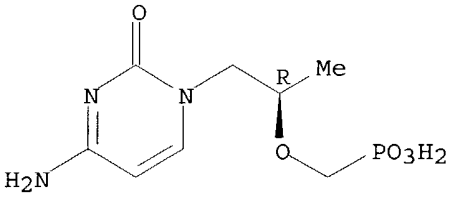
AB Resolved enantiomers of formulas I and its enantiomer II, wherein B is (a) an unsubstituted purine moiety, (b) a substituted purine moiety substituted independently at the 2 and/or 6 and/or 8 position by amino, halogen, hydroxy, alkoxy, alkylamino, dialkylamino, aralkyL-amino, pyrrolidino, morpholino, piperidino, benzoyL-amino, azido, mercapto or alkylthio, or (c) the 8-aza analog thereof, and wherein B is other than guanine or 2-amino-6-halopurine; R is H; and aryl in aralkyL-amino is a 6-10C aromatic group, useful in antiviral pharmaceutical compns. to treat retroviral infections, are prepared via hydrolysis of the appropriate phosphate ester. Thus, 9-(2-phosphono-methoxypropyl)adenine was prepared and was showed in vivo markedly inhibitory to retro-virus replication at 1-2 μg/mL and non-toxic to the cells at 100 μg/mL. In an in vitro study compds. I and II had an EC50 of 1.7 and 1.4 μg/mL, resp., against HIV-1- and HIV-2-induced cytopathicity in human lymphocyte MT-4 cells. Most of the resolved compds. I examined showed marked anti-HIV activity in vitro. HIV-1 and HIV-2 did not differ in their sensitivity to the test compds. Its selectivity index (ratio cytotoxic dose/antiviral active dose) proved superior over that of the prototype compound 9-(2-phosphono-methoxyethyl)adenine (PMEA). The (S)-enantiomer of PMEA was devoid of marked anti-retroviral activity.

IT **160616-05-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of antiretroviral enantiomeric nucleotide analogs)

RN 160616-05-7 HCAPLUS

CN Phosphonic acid, [[(1R)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-methylethoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib abs hitstr l71 2-45

L71 ANSWER 2 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:901829 HCAPLUS
DOCUMENT NUMBER: 140:217930
TITLE: Synthesis and molecular structure of new acyclic analogues of nucleotides with a 1,2-alkadienic

skeleton

AUTHOR(S): Brel, Valery K.; Belsky, Vitaly K.; Stash, Adam I.; Zavodnik, Valery E.; Stang, Peter J.

CORPORATE SOURCE: Institute of Physiologically Active Compounds, Russian Academy of Sciences, Chernogolovka, Moscow Region, 142432, Russia

SOURCE: Organic & Biomolecular Chemistry (2003), 1(23), 4220-4226
CODEN: OBCRAK; ISSN: 1477-0520

PUBLISHER: Royal Society of Chemistry

DOCUMENT TYPE: Journal

LANGUAGE: English

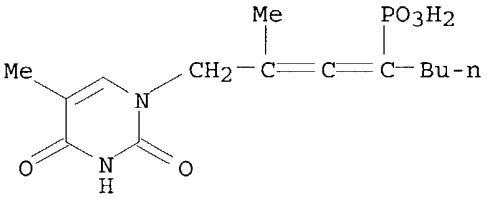
AB Reaction of 1-chloro-4-(diethoxyphosphonyl)alka-2,3-dienes with purine and pyrimidine heterocyclic bases in the presence of cesium carbonate afforded new acyclic analogs of nucleotides containing a 1,2-alkadienic skeleton (I). Dealkylation of I furnished phosphonic acids. In contrast, alkylation reaction with 1-chloro-4-(diethoxyphosphonyl)octa-2,3-diene led to Z- and E- 1,3-alkadienic phosphonates. A similar reaction with 1-chloro-4-(diethoxyphosphonyl)-2-methylbuta-2,3-diene led to the elimination of hydrochloride and formation of 4-(diethylphosphonyl)-2-methylbut-1-en-3-yne. Mol. structures of new acyclic nucleotides are determined by X-ray crystallog. anal.

IT **664372-69-4P**

RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (crystal structure of; synthesis and mol. structure of purine and pyrimidine acyclic nucleotide analogs containing the 1,2-alkadienic skeleton)

RN 664372-69-4 HCAPLUS

CN Phosphonic acid, [1-[3-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-methyl-1-propenylidene]pentyl]- (9CI) (CA INDEX NAME)

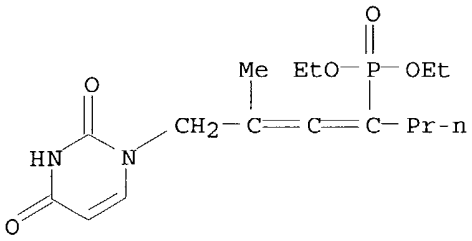


IT **664372-55-8P 664372-56-9P 664372-58-1P 664372-59-2P**

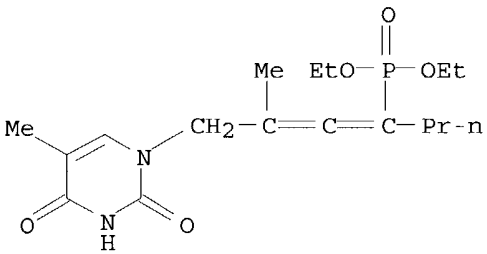
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (synthesis and mol. structure of purine and pyrimidine acyclic nucleotide analogs containing the 1,2-alkadienic skeleton)

RN 664372-55-8 HCAPLUS

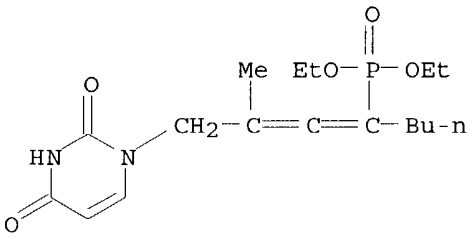
CN Phosphonic acid, [4-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-3-methyl-1-propyl-1,2-butadienyl]-, diethyl ester (9CI) (CA INDEX NAME)



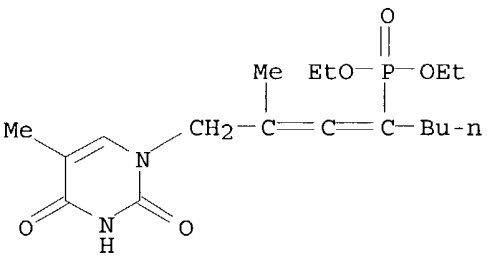
RN 664372-56-9 HCAPLUS
CN Phosphonic acid, [4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-3-methyl-1-propyl-1,2-butadienyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 664372-58-1 HCAPLUS
CN Phosphonic acid, [1-[3-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-2-methyl-1-propenylidene]pentyl]-, diethyl ester (9CI) (CA INDEX NAME)



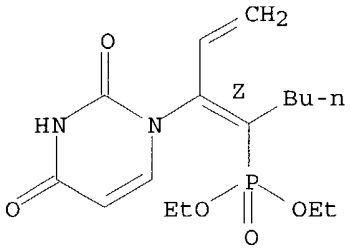
RN 664372-59-2 HCAPLUS
CN Phosphonic acid, [1-[3-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-methyl-1-propenylidene]pentyl]-, diethyl ester (9CI) (CA INDEX NAME)



IT **664372-60-5P 664372-61-6P 664372-62-7P**
664372-63-8P 664372-65-0P 664372-66-1P
664372-68-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis and mol. structure of purine and pyrimidine acyclic nucleotide analogs containing the 1,2-alkadienic skeleton)

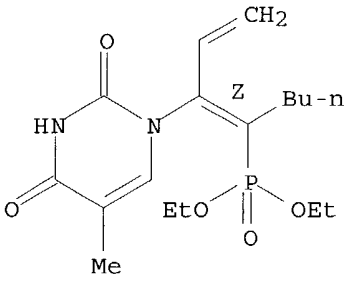
RN 664372-60-5 HCAPLUS
CN Phosphonic acid, [(1Z)-1-[1-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-2-propenylidene]pentyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



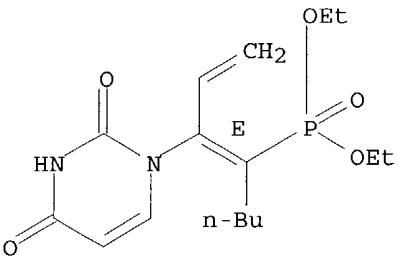
RN 664372-61-6 HCAPLUS
CN Phosphonic acid, [(1Z)-1-[1-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-propenylidene]pentyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 664372-62-7 HCAPLUS
CN Phosphonic acid, [(1E)-1-[1-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-2-propenylidene]pentyl]-, diethyl ester (9CI) (CA INDEX NAME)

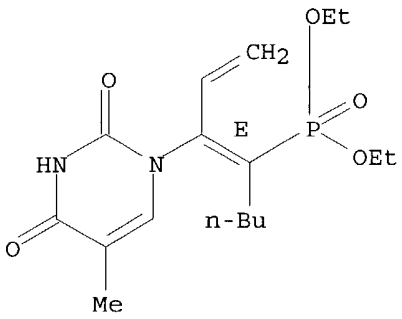
Double bond geometry as shown.



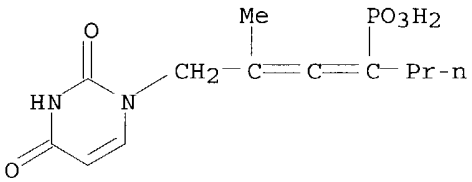
RN 664372-63-8 HCAPLUS

CN Phosphonic acid, [(1E)-1-[1-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-propenylidene]pentyl]-, diethyl ester (9CI) (CA INDEX NAME)

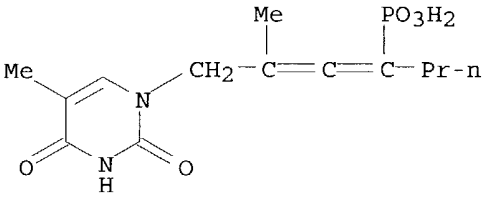
Double bond geometry as shown.



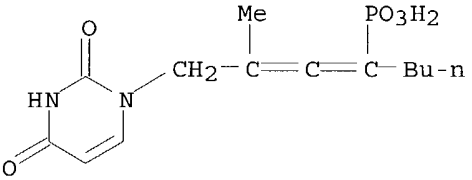
RN 664372-65-0 HCAPLUS
CN Phosphonic acid, [4-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-3-methyl-1-propyl-1,2-butadienyl]- (9CI) (CA INDEX NAME)



RN 664372-66-1 HCAPLUS
CN Phosphonic acid, [4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-3-methyl-1-propyl-1,2-butadienyl]- (9CI) (CA INDEX NAME)

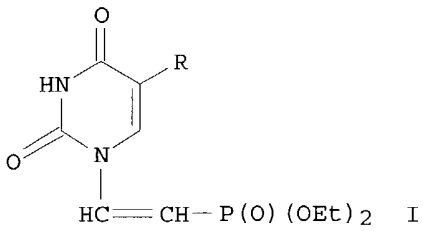


RN 664372-68-3 HCAPLUS
CN Phosphonic acid, [1-[3-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-2-methyl-1-propenylidene]pentyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 3 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:910557 HCAPLUS
DOCUMENT NUMBER: 134:280902
TITLE: Synthesis of new bis-alkylated phosphono alkenyl acyclonucleosides: (Z) and (E)-diethyl-2-(3-alkylpyrimidin-1-yl)ethylen-1-yl phosphonate
AUTHOR(S): Rochdi, A.; Taourirte, M.; Lazrek, H. B.; Barascut, J. L.; Imbach, J. L.
CORPORATE SOURCE: Laboratoire de Chimie Bioorganique, Faculte des Sciences Semlalia, Marrakech, Morocco
SOURCE: Molecules [online computer file] (2000), 5(10), 1139-1145
CODEN: MOLEFW; ISSN: 1420-3049
URL: http://www.mdpi.org/molecules/papers/51001139.pdf
PUBLISHER: Molecular Diversity Preservation International
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:280902
GI



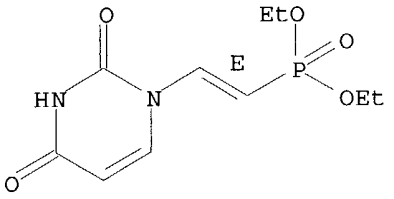
I

AB The E- and Z- phosphonoalkenyl acyclonucleosides of uracil and thymine (shown as I; R = H, Me) were alkylated at the N-3 position of the pyrimidine moiety using K2CO3 and organic bromides (BrCH2CO2Et, BrCH2CH:CH2 and BrCH2C.tplbond.CH) in DMF. The products were tested for their in vitro inhibitory effects on the replication of a number of DNA viruses (ie. herpes simplex virus type 1 and type 2, vaccina virus...) and RNA viruses (Sindbis virus, Coxsackie virus, polio virus,...) in two cell systems (Vero and Hela). None of these compds. showed marked antiviral effect or detectable alteration of host-cell morphol. at the concentration tested (CMI >400 μg/mL). When evaluation in anti-HIV assay (CEM host-cell), none of the tested compds. showed marked antiviral effect at a concentration of <8 μg/mL.

IT **180717-85-5**, (E)-Diethyl (2-(uracil-1-yl)ethenyl)phosphonate
180717-86-6, (Z)-Diethyl (2-(uracil-1-yl)ethenyl)phosphonate
180717-89-9, (E)-Diethyl (2-(thymin-1-yl)ethenyl)phosphonate
180717-90-2, (Z)-Diethyl (2-(thymin-1-yl)ethenyl)phosphonate
RL: RCT (Reactant); RACT (Reactant or reagent)
(N-alkylation of)

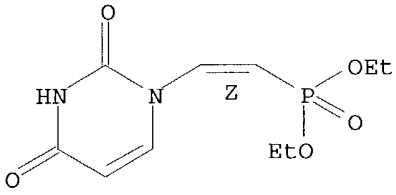
RN 180717-85-5 HCAPLUS
CN Phosphonic acid, [(1E)-2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



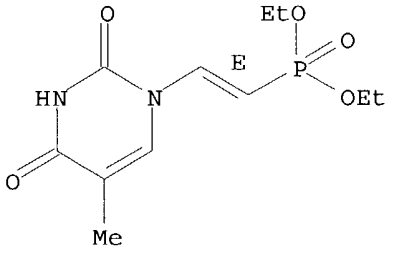
RN 180717-86-6 HCAPLUS
CN Phosphonic acid, [(1Z)-2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



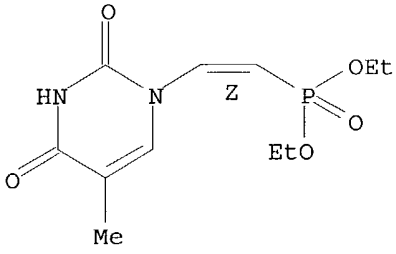
RN 180717-89-9 HCAPLUS
CN Phosphonic acid, [(1E)-2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 180717-90-2 HCAPLUS
CN Phosphonic acid, [(1Z)-2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



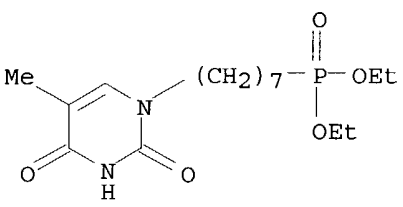
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 4 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:96284 HCAPLUS
DOCUMENT NUMBER: 132:305019
TITLE: Design, Synthesis, and Enzymatic Evaluation of Multisubstrate Analogue Inhibitors of Escherichia coli Thymidine Phosphorylase
AUTHOR(S): Esteban-Gamboa, Antonio; Balzarini, Jan; Esnouf, Robert; De Clercq, Erik; Camarasa, Maria-Jose; Perez-Perez, Maria-Jesus
CORPORATE SOURCE: Instituto de Quimica Medica, C.S.I.C., Madrid, 28006, Spain
SOURCE: Journal of Medicinal Chemistry (2000), 43(5), 971-983
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

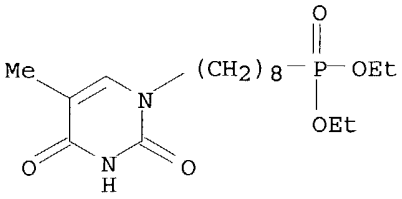
AB A series of acyclic phosphonate derivs. of thymine has been synthesized and tested as multisubstrate analog inhibitors of Escherichia coli thymidine phosphorylase. The compds. synthesized include 1-(phosphonoalkyl)thymines with six to nine methylenes (1-4, resp.); 1-[(Z)-4-phosphonomethoxy-2-butenyl]thymine (5) and its Bu and 2,3-cis-dihydroxybutyl derivs. (6 and 7, resp.); 1-[(Z)-(4-(phosphonomethoxy)methoxy)-2-butenyl]thymine (8) and also its Bu and 2,3-cis-dihydroxybutyl analogs (9 and 10); and 1-[((Z)-4-(phosphonomethoxy)-2-butenoxy)methyl]thymine (11). Evaluation of these compds. against E. coli revealed significant enzymic inhibition by 2, 3, 4, 6, and 8 at a concentration of 1000 μM, 3 and 4 being the most potent. Replacement of the thymine base in 3 by 6-amino-5-bromouracil and 7-deazaxanthine afforded compds. 12 and 13, which showed a pronounced improvement of TPase inhibition, comparable to 7-deazaxanthine. When inorg. phosphate was used as a variable substrate, compds. 12 and 13 displayed competitive kinetics with respect to phosphate, indicating a direct interaction of these compds. with the phosphate binding site. Also compds. 12 and 13 were found to be competitive inhibitors of TPase against thymidine as a variable substrate. These results are consistent with the compds. being multisubstrate analog inhibitors of E. coli TPase, and they represent the first example of such TPase inhibitors.

IT **265322-86-9P 265322-87-0P 265322-88-1P**
265322-89-2P 265322-92-7P 265322-93-8P
265322-99-4P 265323-00-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis, and enzymic evaluation of multisubstrate analog inhibitors of thymidine phosphorylase)

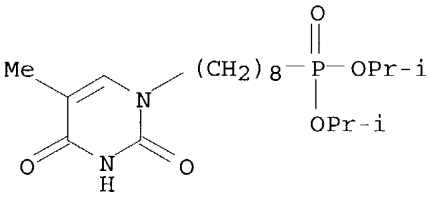
RN 265322-86-9 HCAPLUS
CN Phosphonic acid, [7-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)heptyl]-, diethyl ester (9CI) (CA INDEX NAME)



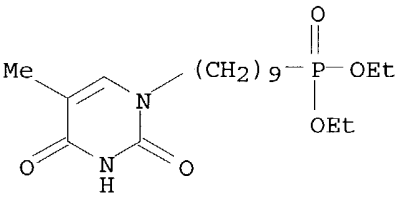
RN 265322-87-0 HCAPLUS
CN Phosphonic acid, [8-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)octyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 265322-88-1 HCAPLUS
CN Phosphonic acid, [8-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)octyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)

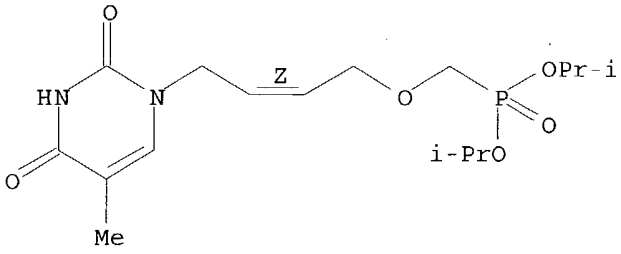


RN 265322-89-2 HCAPLUS
CN Phosphonic acid, [9-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)nonyl]-, diethyl ester (9CI) (CA INDEX NAME)

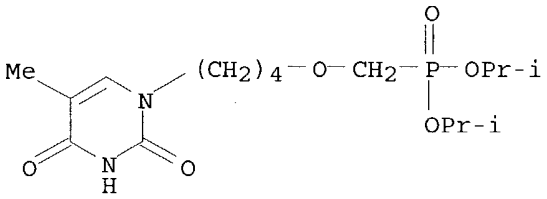


RN 265322-92-7 HCAPLUS
CN Phosphonic acid, [[[(2Z)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

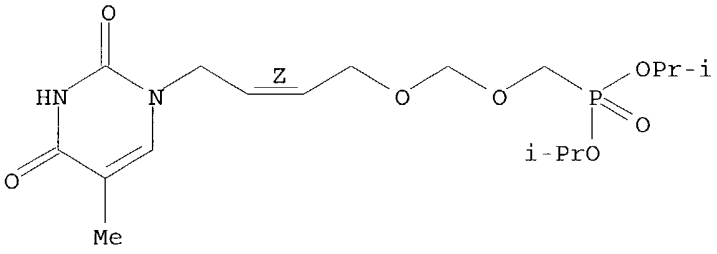


RN 265322-93-8 HCAPLUS
CN Phosphonic acid, [[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)butoxy]methyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)

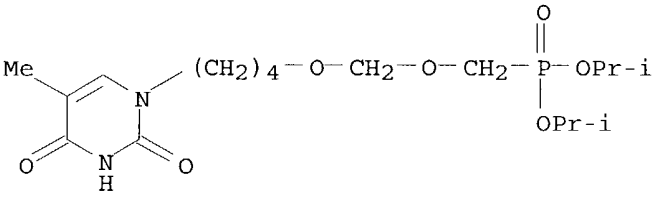


RN 265322-99-4 HCAPLUS
CN Phosphonic acid, [[[[(2Z)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methoxy]methyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

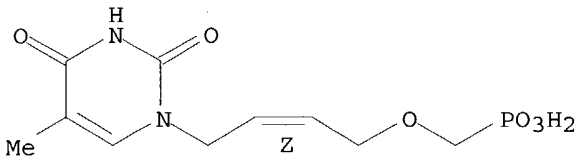


RN 265323-00-0 HCAPLUS
CN Phosphonic acid, [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)butoxy]methoxy]methyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)



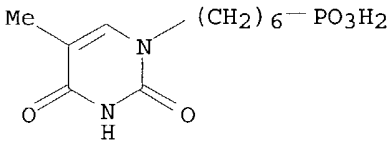
IT **164212-04-8P 265322-73-4P 265322-74-5P**
265322-75-6P 265322-76-7P 265322-77-8P
265322-79-0P 265322-80-3P 265322-82-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(design, synthesis, and enzymic evaluation of multisubstrate analog inhibitors of thymidine phosphorylase)
RN 164212-04-8 HCAPLUS
CN Phosphonic acid, [[[(2Z)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)

Double bond geometry as shown.



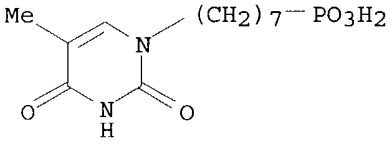
● NH_3

RN 265322-73-4 HCAPLUS
CN Phosphonic acid, [6-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)hexyl]-, monoammonium salt (9CI) (CA INDEX NAME)



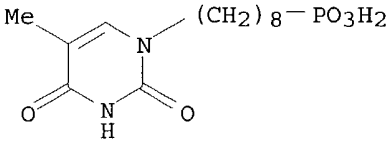
● NH_3

RN 265322-74-5 HCAPLUS
CN Phosphonic acid, [7-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)heptyl]-, monoammonium salt (9CI) (CA INDEX NAME)



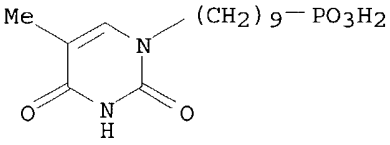
● NH_3

RN 265322-75-6 HCAPLUS
CN Phosphonic acid, [8-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)octyl]-, monoammonium salt (9CI) (CA INDEX NAME)



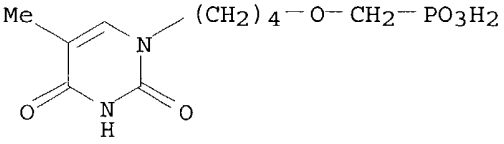
● NH_3

RN 265322-76-7 HCAPLUS
CN Phosphonic acid, [9-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)nonyl]-, monoammonium salt (9CI) (CA INDEX NAME)



● NH_3

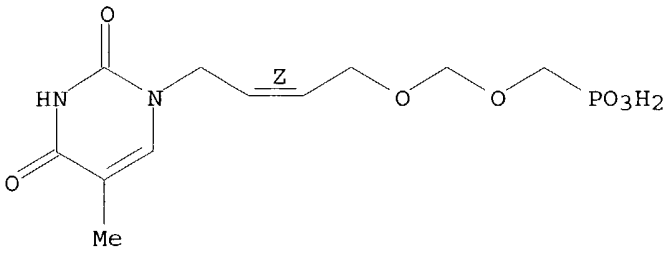
RN 265322-77-8 HCAPLUS
CN Phosphonic acid, [[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)butoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)



● 2 Na

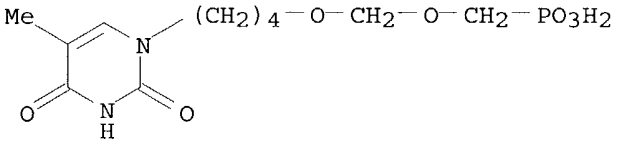
RN 265322-79-0 HCAPLUS
CN Phosphonic acid, [[[[(2Z)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methoxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)

Double bond geometry as shown.



● NH_3

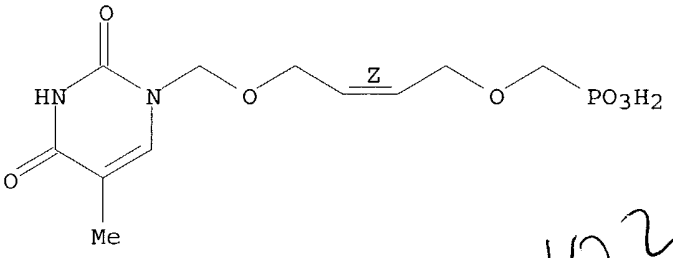
RN 265322-80-3 HCAPLUS
CN Phosphonic acid, [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)butoxy]methoxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)



● NH_3

RN 265322-82-5 HCAPLUS
CN Phosphonic acid, [[[(2Z)-4-[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]-2-butenyl]oxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)

Double bond geometry as shown.



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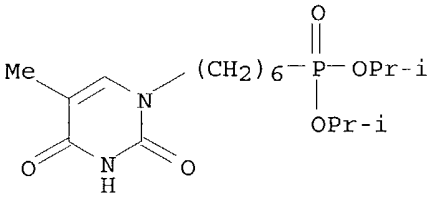
● NH_3

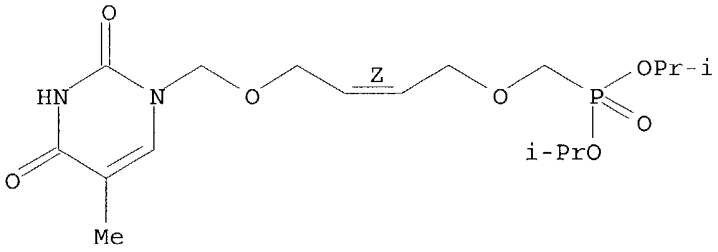
IT **265322-85-8P 265323-03-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(design, synthesis, and enzymic evaluation of multisubstrate analog

inhibitors of thymidine phosphorylase)
RN 265322-85-8 HCAPLUS
CN Phosphonic acid, [6-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)hexyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)



RN 265323-03-3 HCAPLUS
CN Phosphonic acid, [[[(2Z)-4-[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]-2-butenyl]oxy]methyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



102

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

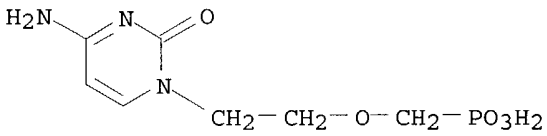
L71 ANSWER 5 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:327297 HCAPLUS
DOCUMENT NUMBER: 131:45038
TITLE: Metal ion-binding properties of the nucleotide analogue 1-[2-(phosphonomethoxy)ethyl]cytosine (PMEC) in aqueous solution
AUTHOR(S): Blindauer, Claudia A.; Holy, Antonin; Sigel, Helmut
CORPORATE SOURCE: Institute of Inorganic Chemistry, University of Basel, Basel, CH-4056, Switz.
SOURCE: Collection of Czechoslovak Chemical Communications (1999), 64(4), 613-632
CODEN: CCCCAK; ISSN: 0010-0765
PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The acidity consts. of the twofold protonated nucleotide analog 1-[2-(phosphonomethoxy)ethyl]cytosine, H2(PMEC)+, as well as the stability consts. of the M(H;PMEC)+ and M(PMEC) complexes with the metal ions MZ+ = Mg2+, Ca2+, Sr2+, Ba2+, Mn2+, Co2+, Ni2+, Cu2+, Zn2+, and Cd2+ have been determined by potentiometric pH titrns. in aqueous solution at I = 0.1 M (NaNO3) and 25°C. Comparison with previous results for the nucleobase-free compound (phosphonomethoxy)ethane, PME, and the parent nucleotides CMP

(CMP2-) and 2'-deoxycytidine 5'-monophosphate (dCMP2-) shows that the metal ion-binding properties of PMEC2- resemble closely those of PME2-: This means, the primary binding site is the phosphonate group and with all of the metal ions studied, 5-membered chelates involving the ether oxygen of the -CH2-O-CH2-PO2-3 chain are formed. The position of the isomeric equilibrium between these chelates and the "open" complexes, -PO2-3/M2+ is calculated; the degree of formation of the chelates is identical within the error limits for the M(PME) and M(PMEC) systems. Hence, like in M(CMP) and M(dCMP) no interaction occurs with the cytosine residue in the M(PMEC) complexes. However, the mono-protonated M(H;PMEC)+ as well as the M(H;CMP)+ and M(dCMP)+ species carry the metal ion predominantly at the nucleobase, while the proton is at the phosphonate group. The coordinating properties of PMEC2- and CMP2- or dCMP2- differ thus only with respect to the possible formation of the 5-membered chelates involving the ether oxygen in M(PMEC) species, a possibility which does not exist in the complexes of the parent nucleotides. Possible reasons why PMEC is devoid of a significant antiviral activity are shortly discussed.

IT **117087-39-5DP**, cation complexes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(metal ion-binding properties of the nucleotide analog 1-[2-(phosphonomethoxy)ethyl]cytosine in aqueous solution)

RN 117087-39-5 HCAPLUS

CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 6 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:322970 HCAPLUS

DOCUMENT NUMBER: 131:73712

TITLE: Structure-Antiviral Activity Relationship in the Series of Pyrimidine and Purine N-[2-(2-Phosphonomethoxy)ethyl] Nucleotide Analogues. 1. Derivatives Substituted at the Carbon Atoms of the Base

AUTHOR(S): Holy, Antonin; Guenter, Jaroslav; Dvorakova, Hana; Masojidkova, Milena; Andrei, Graciela; Snoeck, Robert; Balzarini, Jan; De Clercq, Erik

CORPORATE SOURCE: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, 16610, Czech Rep.

SOURCE: Journal of Medicinal Chemistry (1999), 42(12), 2064-2086
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

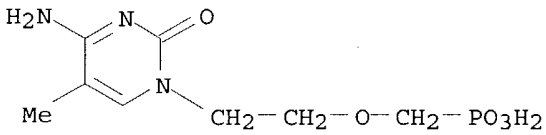
AB Dialkyl esters of purine and pyrimidine N-[2-(phosphonomethoxy)ethyl]

derivs. substituted at position 2, 6, or 8 of the purine base or position 2, 4, or 5 of the pyrimidine base were prepared by alkylation of the appropriate heterocyclic base with 2-chloroethoxymethylphosphonate diester in the presence of NaH, Cs carbonate, or 1,8-diazabicyclo[5,4,0]undec-7-ene (DBU) in DMF. Addnl. derivs. were obtained by the transformations of the bases in the suitably modified intermediates bearing reactive functions at the base moiety. The diesters were converted to the corresponding monoesters by Na azide treatment, while the free acids were obtained from the diester by successive treatment with bromotrimethylsilane and hydrolysis. None of the PME derivs. in the pyrimidine series, their 6-aza or 3-deaza analogs, exhibited any activity against DNA viruses or retroviruses tested, except for the 5-bromocytosine derivative Substitution of the adenine ring in PMEA at position 2 by Cl, F, or OH group decreased the activity against all DNA viruses tested. PMEDAP was highly active against HSV-1, HSV-2, and VZV in the concentration range (EC50) of 0.07-2 μg/mL. Also the 2-amino-6-chloropurine derivative was strongly active (EC50 = 0.1-0.4 μg/mL) against herpes simplex viruses and (EC50 = 0.006-0.3 μg/mL) against CMV and VZV. PMEG was the most active compound of the whole series against DNA viruses (EC50 .apprx.0.01-0.02 μg/mL), though it exhibited significant toxicity against the host cells. The base-modified compds. did not show any appreciable activity against DNA viruses except for 7-deazaPMEA (IC50 .apprx. 7.5 μg/mL) against HIV-1 and MSV. The neutral (diisopropyl, diisooctyl) diesters of PMEA were active against CMV and VZV, while the corresponding monoesters were inactive. The diisopropyl ester of the 2-chloroadenine analog of PMEA showed substantially (10-100+) higher activity against CMV and VZV than the parent phosphonate. Also, the diisopropyl and diisooctyl ester of PMEDAP inhibited CMV and VZV, but esterification of the phosphonate residue did not improve the activity against either MSV or HIV.

IT **113852-44-1**, 5-Methyl-1-[2-(phosphonomethoxy)ethyl]cytosine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antiviral activity of)

RN 113852-44-1 HCAPLUS

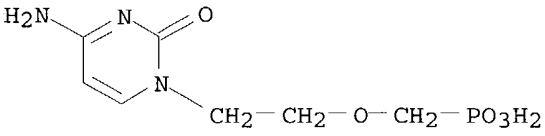
CN Phosphonic acid, [[2-(4-amino-5-methyl-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



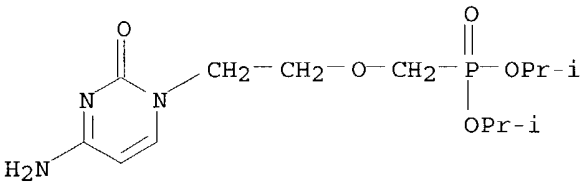
IT **117087-39-5P**, 1-[2-(Phosphonomethoxy)ethyl]cytosine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiviral activity of)

RN 117087-39-5 HCAPLUS

CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



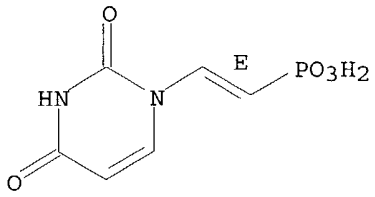
IT **228874-11-1P**, Bis(2-propyl) 1-[2-(Phosphonomethoxy)ethyl]cytosine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, bromination and hydrolysis of)
RN 228874-11-1 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, bis(1-methylethyl) ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 122 THERE ARE 122 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

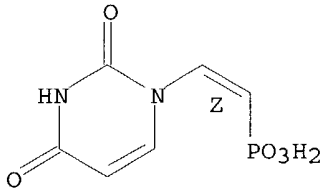
L71 ANSWER 7 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:289928 HCAPLUS
DOCUMENT NUMBER: 128:294984
TITLE: Synthesis of (Z) and (E) α-alkenyl phosphonic acid derivatives of purines and pyrimidines
AUTHOR(S): Lazrek, H. B.; Rochdi, A.; Khaider, H.; Barascut, J.-L.; Imbach, J.-L.; Balzarini, J.; Witvrouw, M.; Pannecouque, C.; De Clercq, E.
CORPORATE SOURCE: Laboratoire de Chimie Bio-Organique, Faculte des Sciences Semlalia, Marrackeh, Morocco
SOURCE: Tetrahedron (1998), 54(15), 3807-3816
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB (Z) and (E)-2-(purin-9-yl/pyrimidin-1-yl)ethylen-1-ylphosphonic acids were synthesized by Michael addition of heterocyclic base with the diethylethynylphosphonate and deprotection of the acyclic nucleoside phosphonate with bromotrimethylsilane. Compds. were tested for their antiviral and cytotoxic activity.
IT **168975-01-7P 168975-02-8P 168975-03-9P**
168975-04-0P 168975-05-1P 168975-06-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of (Z) and (E) alkenyl phosphonic acid derivs. of purines and pyrimidines)
RN 168975-01-7 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



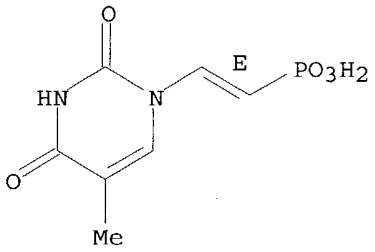
RN 168975-02-8 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



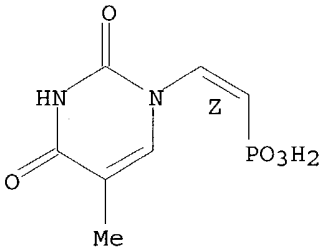
RN 168975-03-9 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



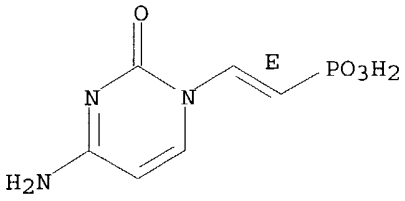
RN 168975-04-0 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



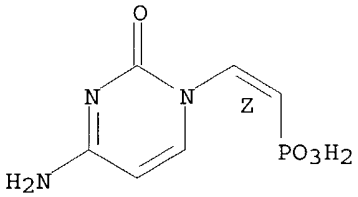
RN 168975-05-1 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



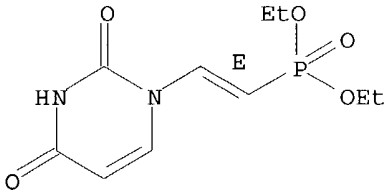
RN 168975-06-2 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



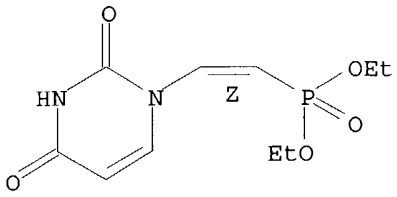
IT **180717-85-5P 180717-86-6P 180717-87-7P**
180717-88-8P 180717-89-9P 180717-90-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of (Z) and (E) alkenyl phosphonic acid derivs. of purines and pyrimidines)
RN 180717-85-5 HCAPLUS
CN Phosphonic acid, [(1E)-2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



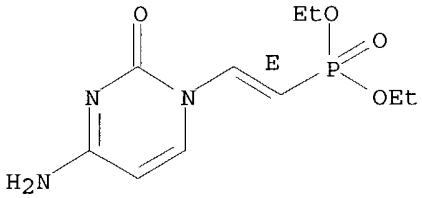
RN 180717-86-6 HCAPLUS
CN Phosphonic acid, [(1Z)-2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



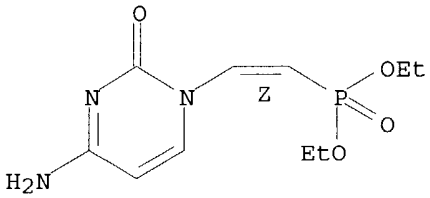
RN 180717-87-7 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



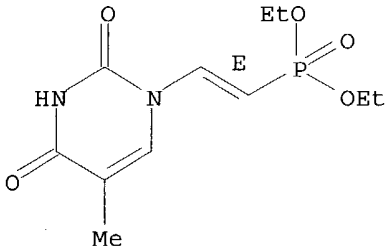
RN 180717-88-8 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



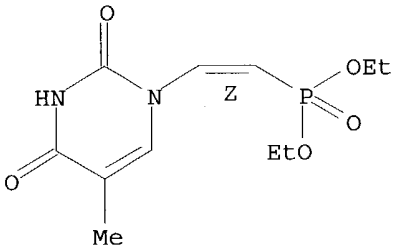
RN 180717-89-9 HCAPLUS
CN Phosphonic acid, [(1E)-2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



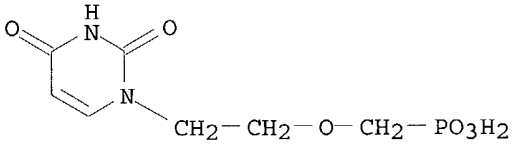
RN 180717-90-2 HCAPLUS
CN Phosphonic acid, [(1Z)-2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

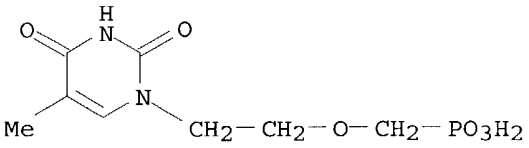


REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

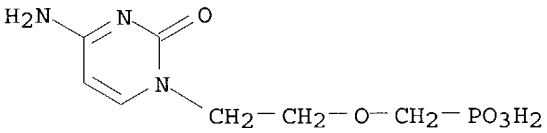
L71 ANSWER 8 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:471688 HCAPLUS
DOCUMENT NUMBER: 127:171040
TITLE: Transport of adefovir (PMEA) in human T-lymphoblastoid cells
AUTHOR(S): Olsanska, Lenka; Cihlar, Tomas; Votruba, Ivan; Holy, Antonin
CORPORATE SOURCE: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, Czech Rep.
SOURCE: Collection of Czechoslovak Chemical Communications (1997), 62(5), 821-828
CODEN: CCCCAK; ISSN: 0010-0765
PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The uptake of [3H]PMEA by human T-lymphoblastoid cells (CCRF-CEM) apparently proceeds by fluid-phase endocytosis. The transport kinetics was shown to be nonconcentrative and nonsaturable. The uptake takes place even at a low temperature (4 °C), is strictly dependent on the intracellular level of ATP, is not substantially affected by cell suspension d. and is not competitively inhibited by other PME derivs.
IT **113852-43-0 116455-16-4 117087-39-5**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(adefovir transport in human T-lymphoblastoid cells)
RN 113852-43-0 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 116455-16-4 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

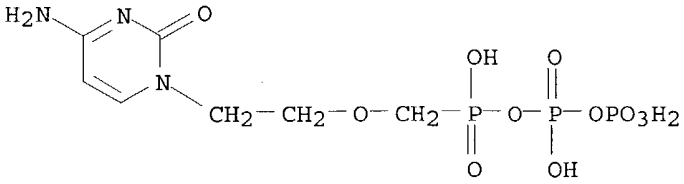


RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

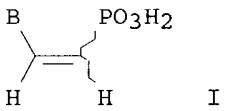


REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L71 ANSWER 9 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:440972 HCAPLUS
DOCUMENT NUMBER: 127:144785
TITLE: (S)-1-(3-Hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC) inhibits HIV-1 replication in epithelial cells, but not T-lymphocytes
AUTHOR(S): Srinivas, Ranga V.; Connely, Michele; Fridland, Arnold
CORPORATE SOURCE: Dep. Infectious Diseases, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA
SOURCE: Antiviral Research (1997), 35(1), 23-27
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB PMEA [9-(2-phosphonylmethoxyethyl)adenine] inhibited both HSV-1 and HIV-1 replication in MT-2 and HeLa-CD4 cells. (S)-1-[3-hydroxy-2-(phosphonylmethoxy)propyl]cytosine (HPMPC) inhibited both these viruses in the epithelioid HeLa-CD4 cells, but did not inhibit either virus in the T-lymphocytic MT-2 cells. PMEA and HPMPC are metabolized to their diphosphorylated forms within cells, which then inhibit viral polymerases. We therefore compared the metabolism of PMEA and HPMPC in MT-2 and HeLa-CD4 cells. PMEApp formation was efficient in both the cell types, whereas HPMPCpp levels were .apprx.3-10 fold lower in MT-2 cells, compared to HeLa-CD4 cells. These results indicate that HPMPC can inhibit HIV replications in the appropriate cell types, and show that differences in their metabolism cannot account entirely for the lack of antiviral efficacy of HPMPC in MT-2 cells.
IT **130029-17-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(effects of (hydroxyphosphonylmethoxyethyl)adenine and (hydroxyphosphonylmethoxypropyl)cytosine on HIV-1 and HSV-1 replication in epithelial cells and T-lymphocytes)
RN 130029-17-3 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)



L71 ANSWER 10 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:427240 HCAPLUS
DOCUMENT NUMBER: 125:196209
TITLE: Synthesis of new acyclic nucleoside phosphonic acids by Michael addition
AUTHOR(S): Lazrek, H. B.; Khaider, H.; Rochdi, A.; Barascut, J.-L.; Imbach, J.-L.
CORPORATE SOURCE: Lab. Chimie Bio-Organique, Faculte Sciences Semlalia, Marrakech, BP S 15, Morocco
SOURCE: Tetrahedron Letters (1996), 37(27), 4701-4704
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 125:196209
GI



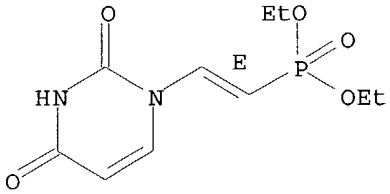
I

AB New acyclic nucleoside phosphonic acids I (adenine, cytosine, N-acetylguanine, thymine, uracil) in the purine and pyrimidine series were prepared via one step by Michael addition These compds. are the first reported acyclic nucleosides enamines which incorporate the α,β-unsatd. phosphonic acid as a phosphate mimic.

IT **180717-85-5P 180717-86-6P 180717-87-7P**
180717-88-8P 180717-89-9P 180717-90-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of new acyclic nucleoside phosphonic acids by Michael addition)

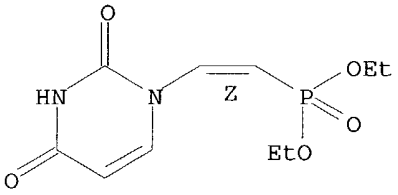
RN 180717-85-5 HCAPLUS
CN Phosphonic acid, [(1E)-2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



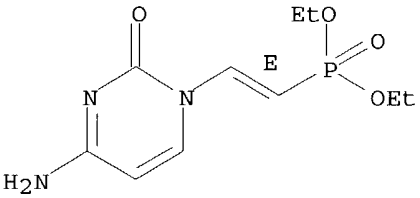
RN 180717-86-6 HCAPLUS
CN Phosphonic acid, [(1Z)-2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



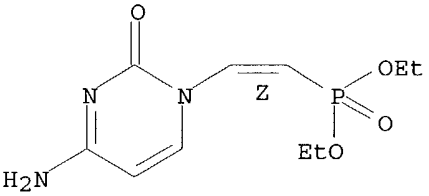
RN 180717-87-7 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



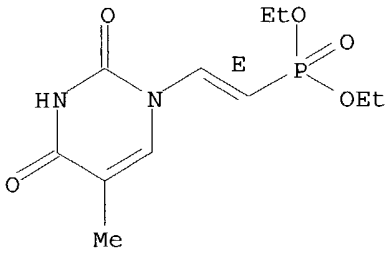
RN 180717-88-8 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



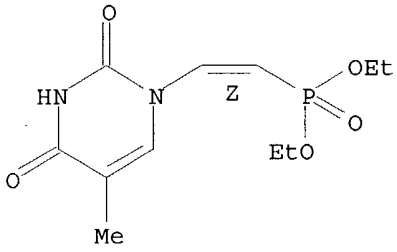
RN 180717-89-9 HCAPLUS
CN Phosphonic acid, [(1E)-2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



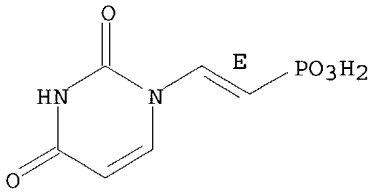
RN 180717-90-2 HCAPLUS
CN Phosphonic acid, [(1Z)-2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, diethyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



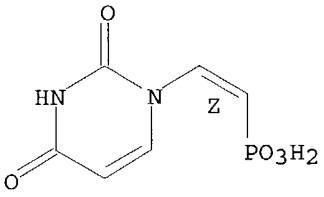
IT **168975-01-7P 168975-02-8P 168975-03-9P**
168975-04-0P 168975-05-1P 168975-06-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of new acyclic nucleoside phosphonic acids by Michael addition)
RN 168975-01-7 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



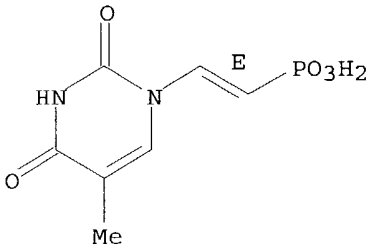
RN 168975-02-8 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



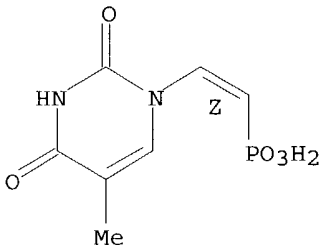
RN 168975-03-9 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



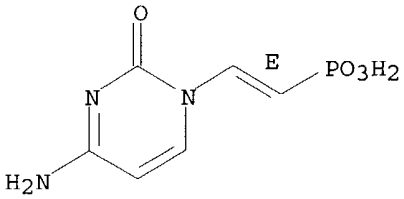
RN 168975-04-0 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 168975-05-1 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

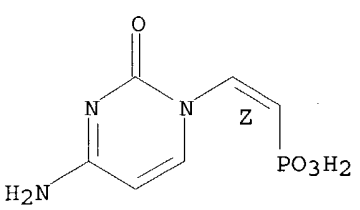
Double bond geometry as shown.



RN 168975-06-2 HCAPLUS

CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



PROV 8

L71 ANSWER 11 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:986491 HCAPLUS
DOCUMENT NUMBER: 124:15494
TITLE: Use of phosphonylmethoxyalkyl nucleosides for the treatment of raised intraocular pressure
INVENTOR(S): Freeman, William R.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9526734	A1	19951012	WO 1995-US4047	19950331
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5468752	A	19951121	US 1994-222128	19940404
CA 2185699	AA	19951012	CA 1995-2185699	19950331
AU 9522037	A1	19951023	AU 1995-22037	19950331
AU 704591	B2	19990429		
EP 754046	A1	19970122	EP 1995-914993	19950331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09511507	T2	19971118	JP 1995-525873	19950331

PRIORITY APPLN. INFO.: US 1994-222128 19940404
US 1994-360995 19941220
WO 1995-US4047 19950331
OTHER SOURCE(S): MARPAT 124:15494

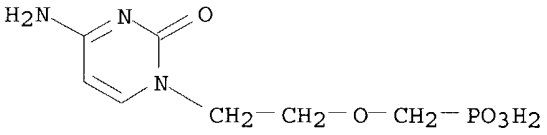
AB A method for reduction of intraocular pressure, especially in glaucoma, comprises administration of phosphonylmethoxyalkyl nucleoside analogs RR1OCH2(CH2)mP(O)R2OH (R = pyrimidine or purine derivative; R = alkyl, alkoxy; R = alkyl, alkoxy, OH; m = 0-3) or their salts. Compns. formulated and packaged for intraocular administration are also provided. Administration of the compound may be by intravitreal injection, aqueous humor injection, injection into the external layer of the eye, such as subconjunctival injection or subtenon injection, or may be, when penetrating derivs. are used, by topical application to the eye. The degree of reduction in

intraocular pressure is dosage-dependent. A single injection can produce prolonged, and perhaps permanent, lowering of the intraocular pressure. (S)-1-(3-hydroxy-2-phosphonylmethoxypropyl)cytosine (HPMPC) liposomes were prepared and injected into the vitreous cavity of eyes of AIDS patients infected with cytomegalovirus at dosage of 10-100 μg/0.1 mL. HPMPC was slowly released from the liposomes over weeks to months, providing gradual decrease in pressure and possibly, if higher dosages are administered, avoiding the need for addnl. injections.

IT **117087-39-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. of phosphonylmethoxyalkyl nucleosides for treatment of raised intraocular pressure)

RN 117087-39-5 HCAPLUS

CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



L71 ANSWER 12 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:885823 HCAPLUS

DOCUMENT NUMBER: 124:117829

TITLE: Synthesis of enantiomeric N-(2-phosphonomethoxypropyl) derivatives of purine and pyrimidine bases. I. The stepwise approach

AUTHOR(S): Holy, Antonin; Masojidkova, Milena

CORPORATE SOURCE: Inst. Org. Chem. Biochem., Acad. Sci., Prague, 166 10, Czech Rep.

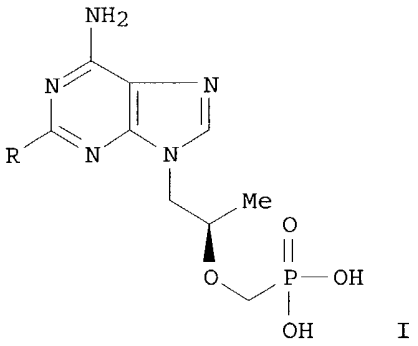
SOURCE: Collection of Czechoslovak Chemical Communications (1995), 60(7), 1196-212
CODEN: CCCCAK; ISSN: 0010-0765

PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I

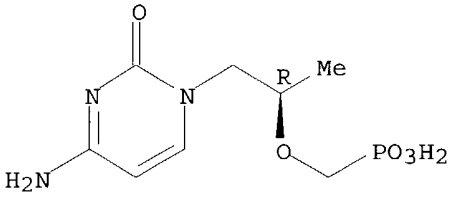
AB Phosphonomethoxypropyl acyclic nucleotide analogs, e.g. I (R = H, NH2), were prepared via alkylation of N-protected N-(2-hydroxypropyl) derivs. of the corresponding bases with bis(2-propyl) p-toluenesulfonyloxymethylphosphonate. This approach was used for the synthesis of cytosine, adenine and 2,6-diaminopurine derivs., while compds. derived from guanine were prepared by hydrolysis of 2-amino-6-chloropurine intermediates.

IT **160616-05-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of phosphonomethoxypropyl acyclic nucleotide analogs via alkylation of nucleoside with propyloxymethylphosphonate)

RN 160616-05-7 HCAPLUS

CN Phosphonic acid, [[(1R)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-methylethoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L71 ANSWER 13 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:835487 HCAPLUS
DOCUMENT NUMBER: 123:257269
TITLE: Preparation of viricidal nucleotide analogs
INVENTOR(S): Bischofberger, Norbert W.; Jones, Robert J.; Arimilli, Murty N.; Lin, Kuei-Ying; Louie, Michael S.; McGee, Lawrence R.; Prisbe, Ernest J.; Lee, William A.; Cundy, Kenneth C.
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 154 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9507920		A1	19950323	WO 1994-US10539	19940916
W:	AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,				
	GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW,				
	NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW:	KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC,				
	NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5656745		A	19970812	US 1993-123483	19930917
CA 2171743		AA	19950323	CA 1994-2171743	19940916
AU 9478752		A1	19950403	AU 1994-78752	19940916
AU 691527		B2	19980521		
EP 719273		A1	19960703	EP 1994-929832	19940916
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9407510		A	19970107	BR 1994-7510	19940916
JP 09506334		T2	19970624	JP 1994-509394	19940916
US 5798340		A	19980825	US 1996-617849	19960506
US 6225460		B1	20010501	US 1999-247497	19990210
US 2001041794		A1	20011115	US 2001-801164	20010307

PRIORITY APPLN. INFO.:

US 1993-123483	A	19930917
US 1994-193341	A	19940208
WO 1994-US10539	W	19940916
US 1996-597005	A2	19960205
US 1996-617849	A3	19960506
US 1998-71420	B1	19980501
US 1999-247497	A1	19990210

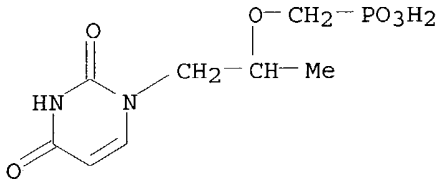
OTHER SOURCE(S): MARPAT 123:257269

GI For diagram(s), see printed CA Issue.

AB Nucleotide analogs [I; B = heterocyclic base; L1, L2 = amino acid or polypeptide residue; Z = (un)substituted 5-membered-ring-containing (un)substituted hydrocarbyl residue; the dotted lines represent facultative bonds], useful as antiviral agents, antitumor agents (no data), and antineoplastic agents (no data), which are further characterized by the presence of an amidate-linked amino acid or an ester-linked group which is bonded to the P atom of phosphonate nucleotide analogs, are prepared and their viricidal activity against HSV-1 and HSV-2 (strain 413-92) viruses presented. I comprise a phosphoamidate or ester bond that is hydrolyzed in vivo to yield a corresponding phosphonate nucleotide analog and methods and intermediates for I synthesis and use are also described.

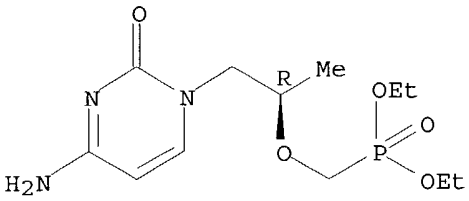
IT **168537-53-9 168537-54-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of viricidal nucleotide analogs from)

RN 168537-53-9 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-1-methylethoxy]methyl]- (9CI) (CA INDEX NAME)

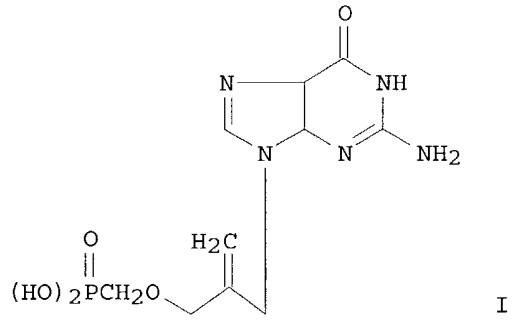


RN 168537-54-0 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-methylethoxy]methyl]-, diethyl ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L71 ANSWER 14 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:666574 HCAPLUS
DOCUMENT NUMBER: 123:340710
TITLE: Synthesis and antiviral activity of rigid acyclonucleotide analogs
AUTHOR(S): Casara, Patrick J.; Altenburger, Jean-Michel; Taylor, Debra L.; Tyms, A. Stanley; Kenny, Michael; Nave, Jean-Francois
CORPORATE SOURCE: Marion Merrell Dow Res. Inst., Strasbourg, 67080, Fr.
SOURCE: Bioorganic & Medicinal Chemistry Letters (1995), 5(12), 1275-80
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

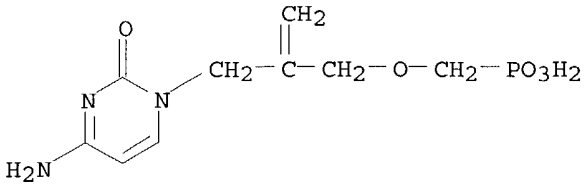


I

AB The synthesis, anti-HIV-1 and anti-herpesvirus activities of new rigid acyclonucleotide analogs are described. 9-[2-Methylidene-3-(phosphonomethoxy)propyl]guanine (I) exhibits in vitro anti-HIV-1 activity similar to that of the antiviral agent 9-[2-(phosphonomethoxy)ethyl]adenine (PMEA). I is 9-fold less toxic to human T-lymphoid cells MT-4 than PMEA.

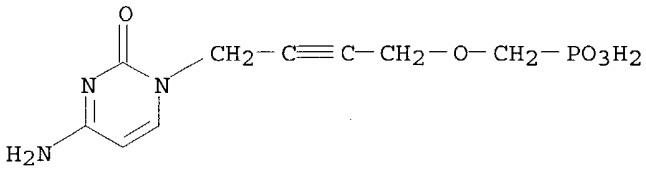
IT **170452-57-0P 170452-59-2P 170452-62-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiviral activity of rigid acyclonucleotide analogs)

RN 170452-57-0 HCAPLUS
CN Phosphonic acid, [[[2-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]- (9CI) (CA INDEX NAME)



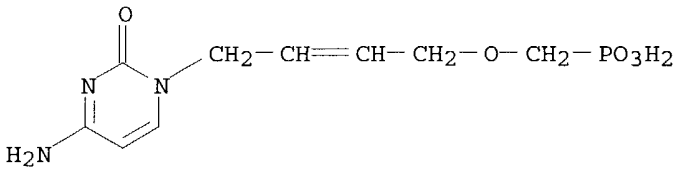
102

RN 170452-59-2 HCAPLUS
CN Phosphonic acid, [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butynyl]oxy]methyl]- (9CI) (CA INDEX NAME)

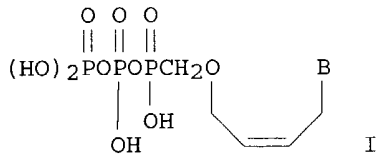


102

RN 170452-62-7 HCAPLUS
CN Phosphonic acid, [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]- (9CI) (CA INDEX NAME)



L71 ANSWER 15 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:631075 HCAPLUS
DOCUMENT NUMBER: 123:286474
TITLE: Novel open-chain nucleotides imitating 2',3'-dideoxy-2',3'-didehydronucleotides: synthesis and substrate properties toward DNA polymerases
AUTHOR(S): Shirokova, E. A.; Tarussova, N. B.; Shipitsin, A. V.; Semizarov, D. G.; Hieber, M.; Krayevsky, A. A.
CORPORATE SOURCE: Engelhardt Inst. of Molecular Biology, Russian Academy of Sciences, Moscow, 117984, Russia
SOURCE: Nucleosides & Nucleotides (1995), 14(3-5), 749-51
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



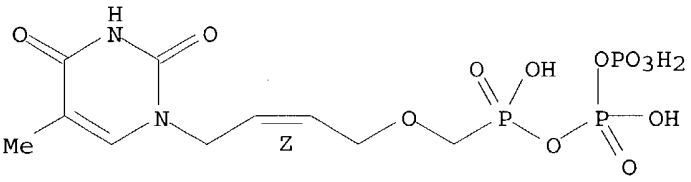
AB Acyclic nucleotide triphosphate isosteres I (B = Ade, Thy, Cyt, Gua) were synthesized and evaluated as potential inhibitors of HIV reverse transcriptases.

IT **163682-64-2P 163682-65-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of acyclic didehydronucleotide analogs and their substrate properties toward DNA polymerases)

RN 163682-64-2 HCAPLUS

CN Diphosphoric acid, monoanhydride with [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]phosphonic acid, (Z)- (9CI) (CA INDEX NAME)

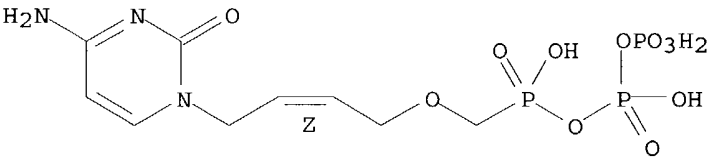
Double bond geometry as shown.



RN 163682-65-3 HCAPLUS

CN Diphosphoric acid, monoanhydride with [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]phosphonic acid, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

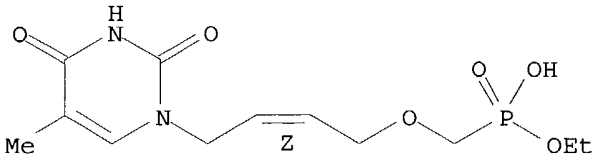


IT **163682-70-0P 163682-74-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of acyclic didehydronucleotide analogs and their substrate properties toward DNA polymerases)

RN 163682-70-0 HCAPLUS

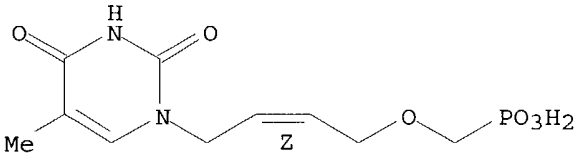
CN Phosphonic acid, [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

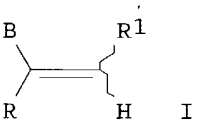


RN 163682-74-4 HCAPLUS
CN Phosphonic acid, [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



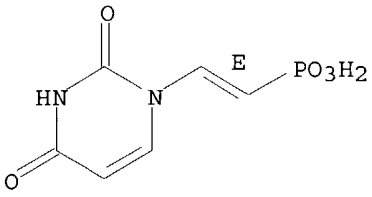
L71 ANSWER 16 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:630991 HCAPLUS
DOCUMENT NUMBER: 123:257207
TITLE: Synthesis of acycloalkenyl derivatives of pyrimidines and purines
AUTHOR(S): Lazrek, H. B.; Redwane, N.; Rochdi, A.; Barascut, J. L.; Imbach, J.-L.; De Clercq, E.
CORPORATE SOURCE: Faculte Sciences Semlalia, Marrakech, Morocco
SOURCE: Nucleosides & Nucleotides (1995), 14(3-5), 353-6
CODEN: NUNUD5; ISSN: 0732-8311
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Conjugate addition of an anionic nucleophile (nucleobase) to an active triple bond (α, β unsatd. carboxylate or phosphonate) was used for preparing α-ethenyl carboxylate or phosphonate derivs. of purines and pyrimidines, e.g. I (B = adenine, cytosine, thymine, uracil; R = H, R1 = PO3H2; R = R1 = CO2Et).
IT **168975-01-7P 168975-02-8P 168975-03-9P**
168975-04-0P 168975-05-1P 168975-06-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of acycloalkenyl nucleosides and nucleotide phosphonates via addition of nucleobases with ethenyl carboxylates or phosphonates)
RN 168975-01-7 HCAPLUS

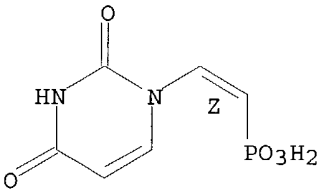
CN Phosphonic acid, [2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



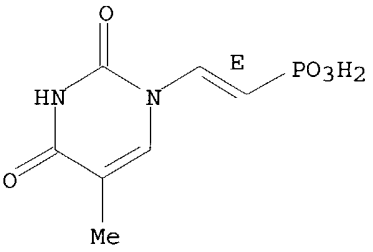
RN 168975-02-8 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



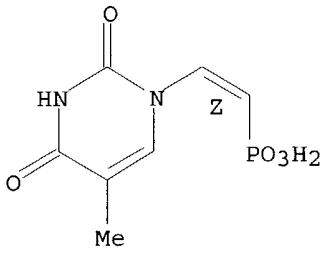
RN 168975-03-9 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



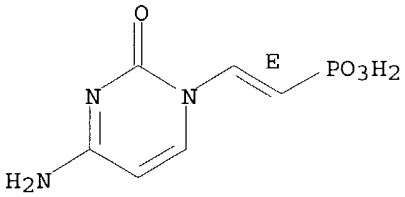
RN 168975-04-0 HCAPLUS
CN Phosphonic acid, [2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



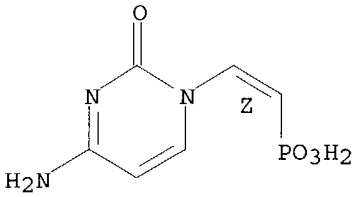
RN 168975-05-1 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 168975-06-2 HCAPLUS
CN Phosphonic acid, [2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethenyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown..

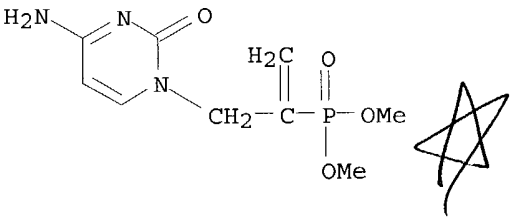


L71 ANSWER 17 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:592491 HCAPLUS
DOCUMENT NUMBER: 123:144033
TITLE: Dimethyl 3-chloroprop-1-en-2-ylphosphonate. Part 2. Alkylation of amines, phosphines and phosphites
AUTHOR(S): Gurevich, Igor E.; Tebby, John C.
CORPORATE SOURCE: Staffordshire Univ., Stoke-on-Trent, ST4 2DE, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1995), (10), 1259-64
CODEN: JCPRB4; ISSN: 0300-922X
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Title compound (MeO)2P(O)C(:CH2)CH2Cl 1 reacted with secondary amines to give 55-87% P-containing allylic amines (MeO)2P(O)C(:CH2)CH2R (R = piperidino, pyrrolidino, morpholino, diethanolamino, NPr2, NiPr2). Interaction of the

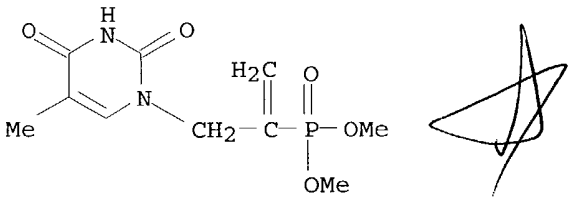
phosphonate 1 with NEt3 formed the corresponding NH4+ salt which, when heated, was converted into betaine MeOP(O)(O-)C(:CH2)CH2N+Et3 20. The reaction of the phosphonate 1 with PPh3 also gave the corresponding phosphonium salt which, when heated, underwent prototropic isomerization to give the betaine MeOP(O)(O-)CMe:CHP+Ph3 22. The phosphonium salt was utilized in a Wittig reaction with paraformaldehyde to form buta-1,3-dien-2-ylphosphonate. The Michaelis-Arbuzov reaction of the phosphonate 1 with tri-Me phosphite led to prop-2-ene-1,2-diyldiphosphonate. Its hydrolysis gave the corresponding diphosphonic acid (HO)2P(O)C(:CH2)CH2P(O)(OH)2 26, which is a hydrolytically stable analog of phosphoenol pyruvate. Alkylation of N-heterocycles, glycine and DL-alanine led to compds. having potential biol. activity (no data).

IT **166906-95-2P 166906-96-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(alkylation of amines, phosphines, and phosphites with (chloropropenyl)phosphonate)

RN 166906-95-2 HCAPLUS
CN Phosphonic acid, [1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]ethenyl]-, dimethyl ester (9CI) (CA INDEX NAME)



RN 166906-96-3 HCAPLUS
CN Phosphonic acid, [1-[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methyl]ethenyl]-, dimethyl ester (9CI) (CA INDEX NAME)



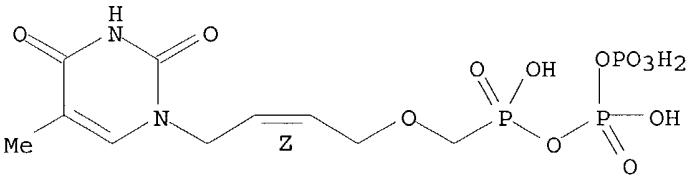
L71 ANSWER 18 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:491175 HCAPLUS
DOCUMENT NUMBER: 123:4274
TITLE: Selectivity of reverse transcriptases. Substrate properties of new acyclic nucleotide analogs
AUTHOR(S): Shirokova, E.; Shipitsin, A.; Semizarov, D.
CORPORATE SOURCE: Engelhardt Inst. Molecular Biology, Russian Academy Sci., Moscow, 117984, Russia
SOURCE: Molekulyarnaya Biologiya (Moscow) (1995), 29(2), 461-71
CODEN: MOBIBO; ISSN: 0026-8984
PUBLISHER: Nauka
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB A new series of nucleotide analogs, (Z)-pyrophosphoryl

(phosphonyloxymethyl)but-2-enyl derivs. of pyrimidines and purines, were synthesized. Their substrate and inhibitory properties toward some DNA polymerases and reverse transcriptases were evaluated. They were shown to be selective inhibitors of HIV reverse transcriptase. The structure-substrate properties relationships for nucleotide analogs were discussed.

IT **163682-64-2P 163682-65-3P 163682-70-0P**
163682-71-1P 163682-74-4P 163682-75-5P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(selectivity of reverse transcriptases and substrate properties of new acyclic nucleotide analogs)

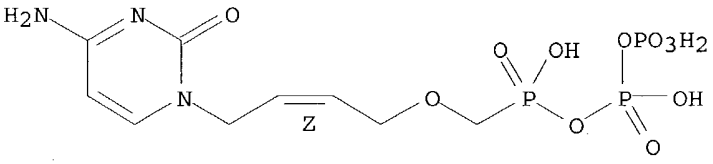
RN 163682-64-2 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]phosphonic acid, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



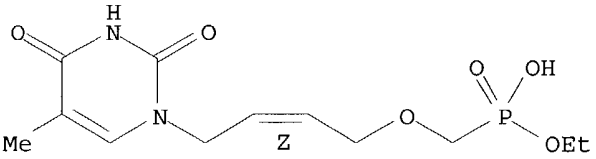
RN 163682-65-3 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]phosphonic acid, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 163682-70-0 HCAPLUS
CN Phosphonic acid, [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoethyl ester, (Z)- (9CI) (CA INDEX NAME)

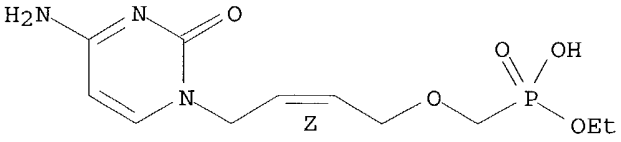
Double bond geometry as shown.



RN 163682-71-1 HCAPLUS

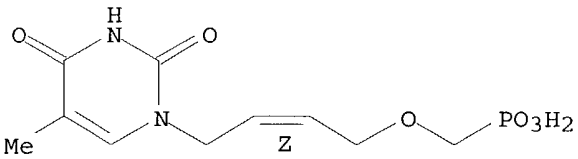
CN Phosphonic acid, [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



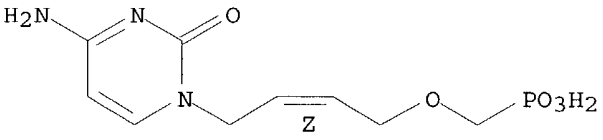
RN 163682-74-4 HCAPLUS
CN Phosphonic acid, [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 163682-75-5 HCAPLUS
CN Phosphonic acid, [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



L71 ANSWER 19 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:390109 HCAPLUS
DOCUMENT NUMBER: 122:177750
TITLE: Antitrypanosomal activity of phosphonylmethoxyalkylpurines
AUTHOR(S): Kaminsky, R.; Zweygarth, E.; Clercq, E. De.
CORPORATE SOURCE: Swiss Tropical Institute, Basel, CH-4002, Switz.
SOURCE: Journal of Parasitology (1994), 80(6), 1026-30
CODEN: JOPAA2; ISSN: 0022-3395
DOCUMENT TYPE: Journal
LANGUAGE: English

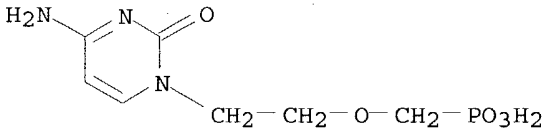
AB Phosphonylmethoxyalkylpurines and -pyrimidines exhibit potent activity against a broad spectrum of DNA viruses. Six of these nucleotide analogs were evaluated for antitrypanosomal activity in vitro and in mice. The most active compds. were (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) and (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)-2,6-diaminopurine (HPMPDAP), which inhibited growth of Trypanosoma brucei brucei by 50% when incubated in vitro for 24 h at 0.23-5.69 μg/mL. Both compds. completely eliminated multidrug-resistant T. b. brucei in culture after 4-5-day exposure at 1 μg/mL. Mice infected with

drug-susceptible T. b. brucei were cured with two 10-mg/kg doses of HPMPDAP. Two or five 50-mg/kg doses of 9-(2-phosphonylmethoxyethyl)adenine (PMEA) or 9-(2-phosphonylmethoxyethyl)-2,6-diaminopurine (PMEDAP), resp., were necessary to eliminate T. b. brucei infections in mice. Mice infected with multidrug-resistant T. b. brucei were not cured with the above dosages. The most active compound against Trypanosoma congolense was PMEDAP, with an EC50 value of 3.21-11.63 μg/mL. Thus, some of the phosphonylmethoxyalkylpurines showed potential as antitrypanosomal compds. at dosages below those toxic for mice.

IT **117087-39-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(trypanosomicidal activity of)

RN 117087-39-5 HCAPLUS

CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

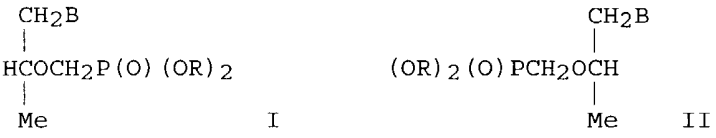


L71 ANSWER 20 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:324493 HCAPLUS
DOCUMENT NUMBER: 122:106401
TITLE: preparation of antiretroviral enantiomeric nucleotide analogs
INVENTOR(S): Holy, Antonin; Dvorakova, Hana; Declercq, Erik Desire Alice; Balzarini, Jan Marie Rene
PATENT ASSIGNEE(S): Institute of Organic Chemistry and Biochemistry, Czech Rep.; Rega Stichting V.Z.W.; Gilead Sciences, Inc.
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9403467	A2	19940217	WO 1993-US7360	19930804
WO 9403467	A3	19940623		
W: CA, CZ, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6057305	A	20000502	US 1992-925610	19920805
EP 654037	A1	19950524	EP 1993-918659	19930804
EP 654037	B1	19990512		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08503927	T2	19960430	JP 1994-505559	19930804
EP 897917	A1	19990224	EP 1998-119443	19930804
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 179983	E	19990515	AT 1993-918659	19930804
ES 2131116	T3	19990716	ES 1993-918659	19930804
CZ 290797	B6	20021016	CZ 1995-272	19930804
CZ 293533	B6	20040512	CZ 2001-529	19930804

US 6653296	B1	20031125	US 1995-379551		19950202
HK 1011998	A1	20001005	HK 1998-113194		19981211
US 6479673	B1	20021112	US 2000-500148		20000208
JP 2004189750	A2	20040708	JP 2004-29994		20040205
PRIORITY APPLN. INFO.:			US 1992-925610	A2	19920805
			EP 1993-918659	A3	19930804
			JP 1994-505559	A3	19930804
			WO 1993-US7360	W	19930804

OTHER SOURCE(S): CASREACT 122:106401; MARPAT 122:106401
GI



I II

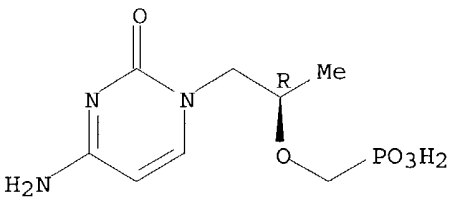
AB Resolved enantiomers of formulas I and II [B is a purine or pyrimidine base; R = H, C1-6 alkyl, aryl, aralkyl] or their aza and/or deaza analogs, useful in antiviral pharmaceutical compns. to treat retroviral infections, are prepared via hydrolysis of the appropriate phosphate ester. E.g., iso-Bu (R)-lactate was protected with 3,4-dihydro-2H-pyran, the resulting iso-Bu (R)-2-O-(tetrahydropyranyl)lactate was reduced with LiAlH4, the resulting 2-O-(tetrahydropyranyl)-(R)-propane-1,2-diol was 1-O-tosylated, the resulting 1-O-tosyl-2-O-(tetrahydropyranyl)propane-1,2-diol was reacted with adenine in DMF containing cesium carbonate and the product was deprotected, the resulting 9-(R)-(2-hydroxypropyl)adenine was first N6-benzoylated and the product was treated with diisopropyl (p-toluenesulfonyloxy)methylphosphonate in DMF containing NaH, the product was deprotected at the N6 position with MeONa-MeOH followed by hydrolysis to give (2'R)-I [B = 9-adeninyl, R = isopropyl]. In an in vitro study this had an EC50 of 1.7 and 1.4 μg/Ml, resp., against HIV-1- and HIV-2-induced cytopathicity in human lymphocyte MT-4 cells.

IT **160616-05-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of, as antiviral)

RN 160616-05-7 HCAPLUS

CN Phosphonic acid, [[(1R)-2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-methylethoxy]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

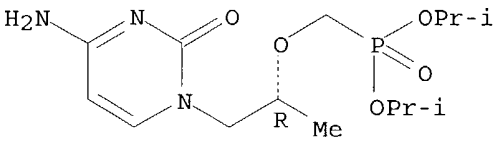


IT **160616-50-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for antivirals)

RN 160616-50-2 HCAPLUS

CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)-1-methylethoxy]methyl]-, bis(1-methylethyl) ester, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



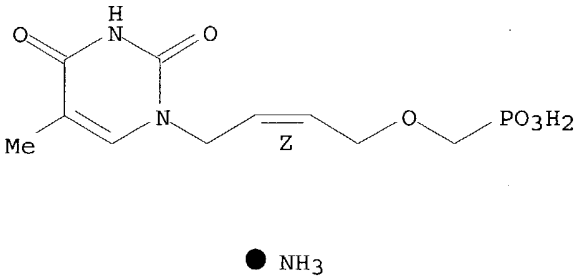
L71 ANSWER 21 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:55077 HCAPLUS
DOCUMENT NUMBER: 123:170042
TITLE: Novel Acyclic Nucleotides and Nucleoside 5'-Triphosphates Imitating 2',3'-Dideoxy-2',3'-didehydro nucleotides: Synthesis and Biological Properties
AUTHOR(S): Shirokova, Elena A.; Tarussova, Natalia B.; Shipitsin, Alexander V.; Semizarov, Dmitry G.; Krayevsky, Alexander A.
CORPORATE SOURCE: V. Engelhardt Institute of Molecular Biology, Moscow, 117984, Russia
SOURCE: Journal of Medicinal Chemistry (1994), 37(22), 3739-48
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English

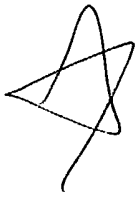
AB A series of pyrophosphoryl (Z)-(phosphonomethoxy)but-2-enyl derivs. of pyrimidines and purines and the corresponding phosphonates were synthesized. The prepared compds. contain the phosphonate group as an α-phosphate mimic as well as an acyclic residue emulating the sugar moiety in 2',3'-dideoxy-2',3'-didehydro nucleoside 5'-triphosphates known as highly potent chain terminators of DNA polymerases. Their substrate properties were evaluated in cell-free systems containing various DNA polymerases including viral reverse transcriptases. These compds. manifested good terminating substrate properties toward HIV-1 and AMV reverse transcriptases. They exhibited high selectivity and were not recognized by human DNA polymerases α and ε, DNA polymerase β from rat liver, Escherichia coli DNA polymerase I, and HSV-1 and CMV DNA polymerases. Phosphonates displayed no activity in HIV-1-infected MT-4 cells cultures; the adenine phosphonate was moderately effective (ED50 = 9 μM).

IT **164212-04-8P 164212-05-9P 164212-08-2P 164212-09-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antiviral activity of acyclic dideoxydidehydro nucleotide triphosphates)

RN 164212-04-8 HCAPLUS
CN Phosphonic acid, [[[(2Z)-4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoammonium salt (9CI) (CA INDEX NAME)

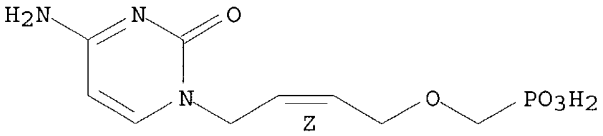
Double bond geometry as shown.

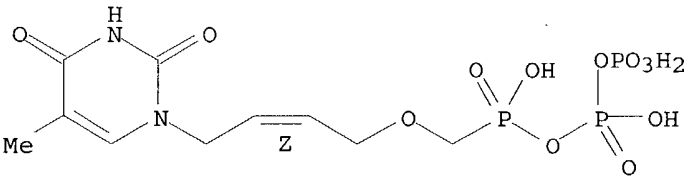




RN 164212-05-9 HCAPLUS
CN Phosphonic acid, [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoammonium salt, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



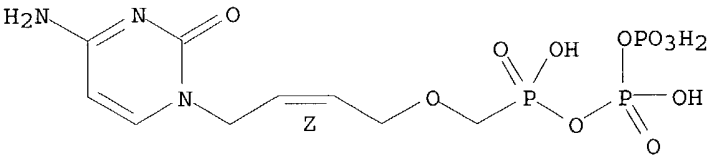


RN 164212-08-2 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]phosphonic acid, diammonium salt, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

RN 164212-09-3 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]phosphonic acid, diammonium salt, (Z)- (9CI) (CA INDEX NAME)

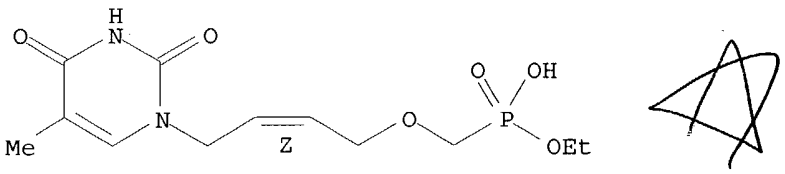
Double bond geometry as shown.



● 2 NH_3

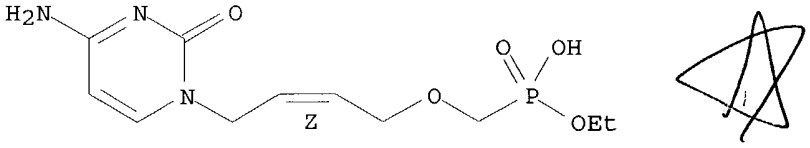
IT **163682-70-0P 163682-71-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antiviral activity of acyclic dideoxydidehydro nucleotide triphosphates)
RN 163682-70-0 HCAPLUS
CN Phosphonic acid, [[[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 163682-71-1 HCAPLUS
CN Phosphonic acid, [[[4-(4-amino-2-oxo-1(2H)-pyrimidinyl)-2-butenyl]oxy]methyl]-, monoethyl ester, (Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

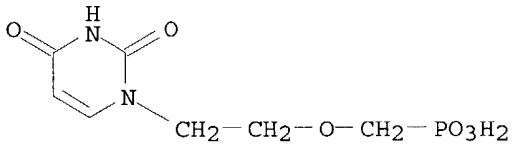


L71 ANSWER 22 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:400268 HCAPLUS
DOCUMENT NUMBER: 121:268
TITLE: Inhibitory effects of acyclic nucleoside phosphonate analogs on hepatitis B virus DNA synthesis in HB611 cells
AUTHOR(S): Yokota, T.; Konno, K.; Shigeta, S.; Holy, A.; Balzarini, J.; De Clercq, E.
CORPORATE SOURCE: Ration. Drug Des. Lab., Fukushima, 960-12, Japan
SOURCE: Antiviral Chemistry & Chemotherapy (1994), 5(2), 57-63
CODEN: ACCHEH; ISSN: 0956-3202
DOCUMENT TYPE: Journal
LANGUAGE: English
AB By using an assay system based on a human hepatoblastoma cell line (HB611)

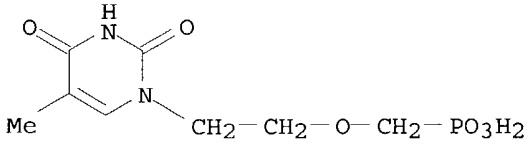
that continuously synthesizes hepatitis B virus (HBV) DNA, 56 acyclic nucleoside phosphonate analogs were examined for their inhibitory effects on HBV DNA synthesis. The following compds. were found to inhibit HBV DNA synthesis at concns. that were significantly lower than their min. cytotoxic concns.; 9-(2-phosphonylmethoxyethyl)adenine (PMEA), 9-(2-phosphonylmethoxyethyl)guanine (PMEG), 9-(2-phosphonylmethoxyethyl) guanine Et ester (PMEGEE), 9-(2-phosphonylmethoxyethyl)-1-deazadenine (PMEC1A), 9-(2-phosphonylmethoxyethyl)-2,6-diaminopurine (PMEDAP), (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA), 9-(3-isopropoxy-2-phosphonylmethoxypropyl)adenine (IPPMPA), 9-(RS)-(2-phosphonylmethoxypropyl)adenine (PMPA) and 9-(3-hydroxy-2-phosphonylmethoxypropyl)-2, 6-diaminopurine (HPMPDAP). The most selective compds. (with indexes greater than 100) were PMEDAP, PMEA, IPPMPA, and PMPA. Acyclic pyrimidine nucleoside phosphonate analogs did not prove markedly selective as anti-HBV agents. Diphosphoryl derivs. of some acyclic purine nucleoside phosphonates (i.e. PMEA, PMEDAP, HPMPA) were prepared They proved inhibitory to HBV DNA polymerase but not cellular DNA polymerase α.

IT **113852-43-0 116455-16-4 117087-39-5 129431-98-7**
RL: BIOL (Biological study)
(hepatitis B virus DNA synthesis inhibition by)

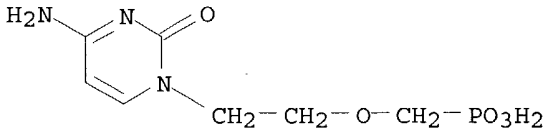
RN 113852-43-0 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 116455-16-4 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

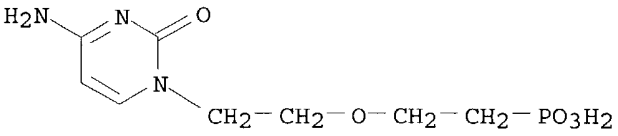


RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 129431-98-7 HCAPLUS
CN Phosphonic acid, [2-[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]ethyl]-

(9CI) (CA INDEX NAME)

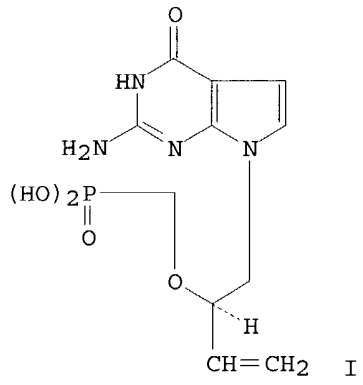


L71 ANSWER 23 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1994:31155 HCAPLUS
DOCUMENT NUMBER: 120:31155
TITLE: Antiviral acyclic phosphonomethoxyalkyl substituted, alkenyl and alkynyl purine and pyrimidine derivatives
INVENTOR(S): Martin, John C.; Bronson, Joanne J.; Yu, Kuo Long
PATENT ASSIGNEE(S): Gilead Sciences, Inc., USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307157	A1	19930415	WO 1992-US8686	19921009
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, NL, PL, RO				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, SE				
AU 9227831	A1	19930503	AU 1992-27831	19921009
AU 661347	B2	19950720		
EP 630381	A1	19941228	EP 1992-922088	19921009
EP 630381	B1	19970409		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
HU 66770	A2	19941228	HU 1994-1002	19921009
JP 07503453	T2	19950413	JP 1993-507233	19921009
JP 3497505	B2	20040216		
AT 151432	E	19970415	AT 1992-922088	19921009
CZ 287745	B6	20010117	CZ 1994-845	19921009
IL 103410	A1	19980104	IL 1992-103410	19921011
NO 9401275	A	19940610	NO 1994-1275	19940408
US 5696263	A	19971209	US 1994-350851	19941206

PRIORITY APPLN. INFO.: US 1991-777835 A 19911011
CS 1994-845 A 19921009
WO 1992-US8686 A 19921009

OTHER SOURCE(S): MARPAT 120:31155
GI



I

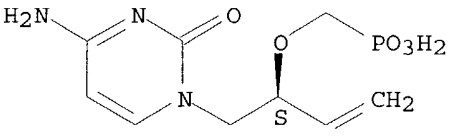
AB Acyclic nucleosides (HO)2P(O)CH2OCHRCH2B (R = alkyl, azidoalkyl, aminoalkyl, alkenyl, alkynyl; B = nucleic acid base) and their salts, esters or racemates were prepared for use as virucides. Thus, (R)-phosphonobutenylguanine I was prepared from (R)-1,2,4-butanetriol via reaction with 4-MeC6H4CH2P(O)(OCHMe2)2, dehydration, reaction with 2-amino-6-chloropurine, and hydrolysis. I has an EC50 against HIV of 12.6 μM and a selectivity index, relative to cytotoxicity of >79.

IT **151223-03-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and virucidal activity)

RN 151223-03-9 HCAPLUS

CN Phosphonic acid, [[[1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

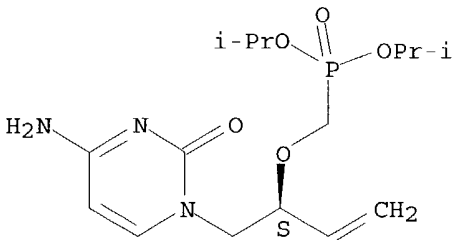


IT **151223-52-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation as intermediate in preparation of virucidal phosphonmethoxyethyl
nucleosides)

RN 151223-52-8 HCAPLUS

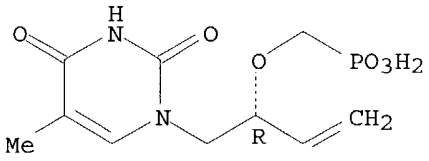
CN Phosphonic acid, [[[1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]-, bis(1-methylethyl) ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



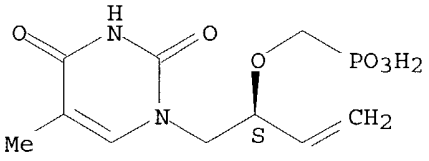
IT **151597-67-0P 151597-68-1P 151597-69-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 151597-67-0 HCAPLUS
CN Phosphonic acid, [[[1-[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



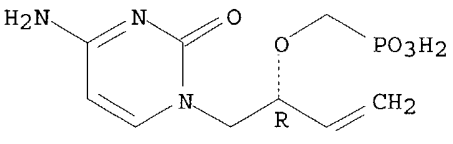
RN 151597-68-1 HCAPLUS
CN Phosphonic acid, [[[1-[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 151597-69-2 HCAPLUS
CN Phosphonic acid, [[[1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L71 ANSWER 24 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1993:671247 HCAPLUS
DOCUMENT NUMBER: 119:271247

TITLE: Synthesis and antiviral activity of 2'-substituted 9-[2-(phosphonomethoxy)ethyl]guanine analogs

AUTHOR(S): Yu, Kuo Long; Bronson, Joanne J.; Yang, Hyekyung; Patick, Amy; Alam, Masud; Brankovan, Vera; Datema, Roelf; Hitchcock, Michael J. M.; Martin, John C.

CORPORATE SOURCE: Pharm. Res. Inst., Bristol-Myers Squibb Co., Wallingford, CT, 06492-7660, USA

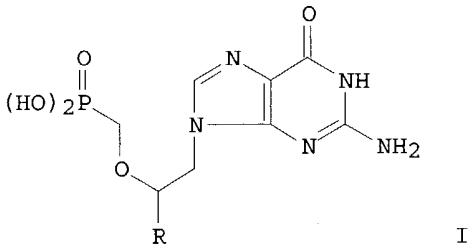
SOURCE: Journal of Medicinal Chemistry (1993), 36(19), 2726-38
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 119:271247

GI



I

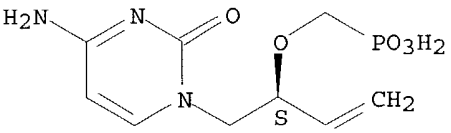
AB A series of 2'-substituted derivs. of 9-[2-(phosphonomethoxy)ethyl]guanine (PMEG, I; R = H) were synthesized and evaluated in vitro for anti-human immunodeficiency virus (HIV) activity in the XTT assay and for anti-herpes activity in the plaque reduction assay. The anti-HIV activity of these derivs. depends on the size and the nature of the substituent as well as the chirality at the 2'-position of PMEG. In addition, these compds. generally demonstrated greater activity against HIV than herpes viruses. The most interesting analogs which emerged from these studies are (R)-2'-(azidomethyl)-PMEG [(R)-I (R = CH2N3)] and (R)-2'-vinyl-PMEG [(R)-I (R = vinyl)]. The former showed anti-HIV activity with an IC50 of 5 μM and a cytotoxicity (CC50) greater than 1.4 mM in CEM cells. The latter has an IC50 of 13 μM for anti-HIV activity and a CC50 of greater than 1.6 mM. Furthermore,it was demonstrated that replacement of the guanine base of these 2'-substituted PMEG analogs with cytosine drastically reduces anti-HIV and anti-herpes activity.

IT **151223-03-9P 151223-05-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and virucidal activity of)

RN 151223-03-9 HCAPLUS

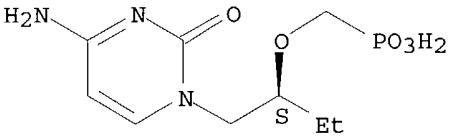
CN Phosphonic acid, [[[1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



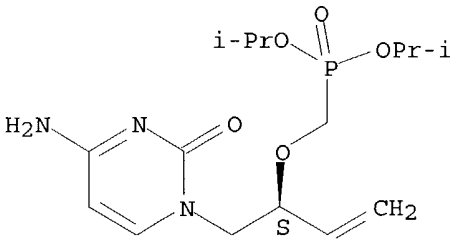
RN 151223-05-1 HCAPLUS
CN Phosphonic acid, [[1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]propoxy]meth yl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



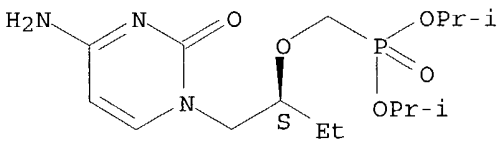
IT **151223-52-8P 151223-54-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate in preparation of substituted chiral [(phosphonomethoxy)ethyl]cytosine analogs)
RN 151223-52-8 HCAPLUS
CN Phosphonic acid, [[[1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]-2-propenyl]oxy]methyl]-, bis(1-methylethyl) ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 151223-54-0 HCAPLUS
CN Phosphonic acid, [[1-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methyl]propoxy]meth yl]-, bis(1-methylethyl) ester, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L71 ANSWER 25 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:592260 HCAPLUS
DOCUMENT NUMBER: 117:192260

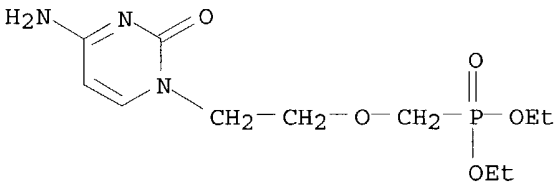
TITLE: Preparation of N-(2-phosphonomethoxy)ethyl derivatives of purine and pyrimidine bases as intermediates for virustats
INVENTOR(S): Rosenberg, Ivan; Holy, Antonin
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 5 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 264223	B1	19890613	CS 1986-5470	19860718

PRIORITY APPLN. INFO.: CS 1986-5470 19860718
OTHER SOURCE(S): MARPAT 117:192260

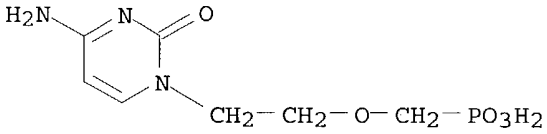
AB BCH2CH2OCH2P(O)(OH)2 (I; B = purin-9-yl, pyrimidin-1-yl residue) and their alkali metal salts were prepared by N-alkylation of Na salts of the parent heterocyclic bases or their -NAc, -NBz, -NCH2NMe2, or -OMe derivs. with 1-1.5 mol equiv (on the base) of BrCH2CH2OCH2P(O)(OH)2 (II) in DMF at 80-120°. The resulting intermediary B'CH2CH2OCH2P(O)(OH)2 (III; B' = B or their -NAc, -NBz, -NCH2NMe2, or -OMe derivative) was separated by chromatog., optionally deprotected by a base, and deesterified by treatment with a trimethylhalosilane. Thus, a mixture of 1.35 g adenine and 0.24 g NaH in 80 mL DMF was stirred 1 h at 80°, treated with stirring over 3 h at that temperature by 2.75 g II [preparation in 60-65% yield by bromination of HOCH2CH2OCH2P(O)(OEt)2 with PPh3/CBr4 given] in 10 mL DMF, and the whole stirred for another 3 h at 80° to gene, after chromatog. on silica gel, 1.4 g III (B' = adenin-9-yl). This was allowed to stand for 16 h at the ambient temperature with a mixture of 36 mL MeCN and 2.4 mL Me3SiBr, the product treated by Et3N in aqueous MeCN and chromatographed to give 85-90% title compound I (B = adenin-9-yl).

IT **120362-31-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deesterification of, by trimethylbromosilane, in preparation of virustat intermediate)
RN 120362-31-4 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)

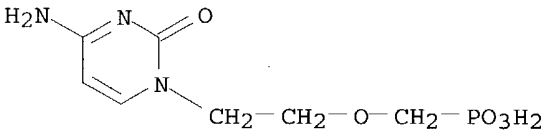


IT **117087-39-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and salification of, in preparation of virustat intermediate)
RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]-

(9CI) (CA INDEX NAME)

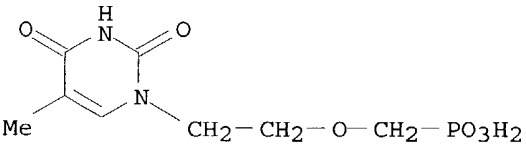


IT **138776-61-1P 138776-62-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as virustat intermediate)
RN 138776-61-1 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

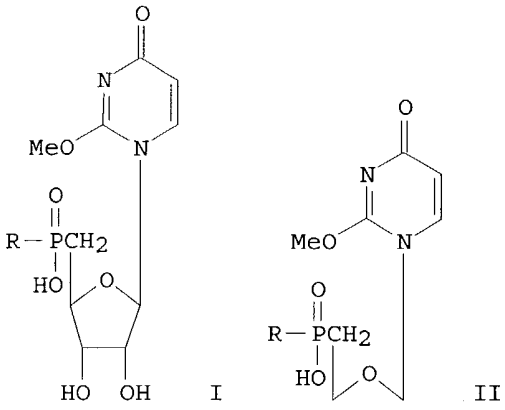
RN 138776-62-2 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L71 ANSWER 26 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:214829 HCAPLUS
DOCUMENT NUMBER: 116:214829
TITLE: Attempted synthesis of 5'-deoxy-5'-phosphonoisocytidine. Synthesis of phosphonic acid derivatives of acyclonucleosides. Preparation of 1-β-D-arabinofuranosyl pyrimidines
AUTHOR(S): Hakimelahi, G. H.; Khalafi-Nezhad, A.
CORPORATE SOURCE: Fac. Sci., Univ. Shiraz, Shiraz, Iran
SOURCE: Journal of Sciences, Islamic Republic of Iran (1990), 1(5), 355-60
CODEN: JSIIEN; ISSN: 1016-1104
DOCUMENT TYPE: Journal

LANGUAGE: English
GI



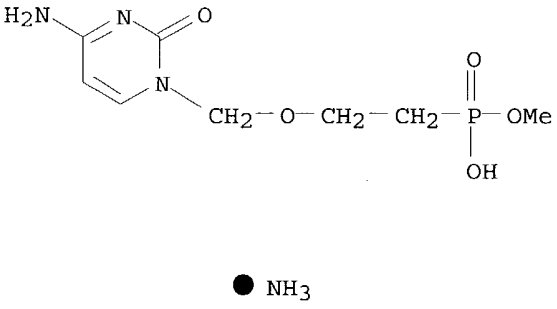
I

II

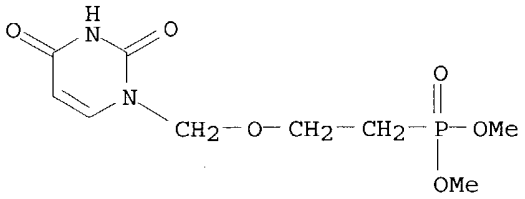
AB The synthesis of 5'-deoxynucleoside 5'-phosphonates, e.g. I (R = OMe, ONH4), which contains a 5'-CP bond in place of the 5'-COP bond of the naturally occurring nucleotides, is described. The preparation of phosphonate derivs. of acyclonucleosides, e.g. II, and a simple method for the conversion of 1-β-D-ribofuranosyl pyrimidines to the corresponding 1-β-D-arabinofuranosyl pyrimidines, are also explained.

IT **141039-34-1P 141039-36-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 141039-34-1 HCAPLUS
CN Phosphonic acid, [2-[(4-amino-2-oxo-1(2H)-pyrimidinyl)methoxy]ethyl]-, monomethyl ester, monoammonium salt (9CI) (CA INDEX NAME)



RN 141039-36-3 HCAPLUS
CN Phosphonic acid, [2-[(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]ethyl]-, dimethyl ester (9CI) (CA INDEX NAME)



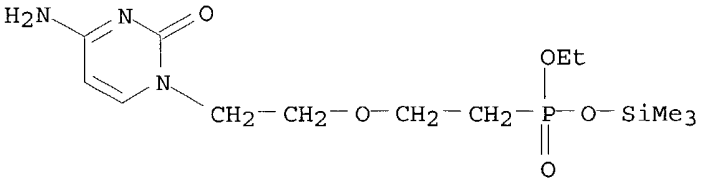
L71 ANSWER 27 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1992:41198 HCAPLUS
DOCUMENT NUMBER: 116:41198
TITLE: Preparation of N-[2-(2-phosphonylethoxy) ethyl] derivatives of heterocyclic bases as insect sterilants
INVENTOR(S): Holy, Antonin; Rosenberg, Ivan; Gelbic, Ivan
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 10 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 270067	B1	19900613	CS 1988-5245	19880721

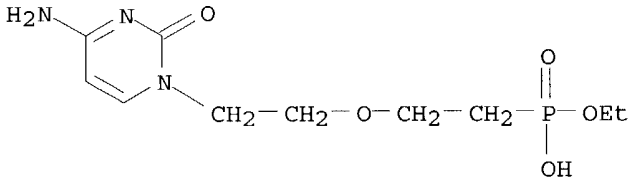
PRIORITY APPLN. INFO.: CS 1988-5245 19880721
OTHER SOURCE(S): MARPAT 116:41198

AB BCH2CH2OCH2CH2P(O)(OR)2 [I; R = H) (II; B = purin-9-yl or purin-7-yl optionally substituted in position 6 by HO, H2N, MeS, or Cl, and in position 2 by H, H2N; uracil-1-yl, cytosin-1-yl) were prepared by N-alkylation of the appropriate bases with the chloroester ClCH2CH2OCH2CH2P(O)(OEt)2 (III) followed by cleavage of the phosphonate ester groups with Me3SiBr in MeCN. Thus, 6.4 g III [preparation from (ClCH2CH2)2O and (EtO)3P given] was added to a prestirred mixture of 3.22 g 6-methylthiopurine and 0.48 g NaH in 80 mL DMF and the whole heated 18 h at 100° to give, after chromatog., 4.0 g intermediate I (R = Et, B = 6-methylthiopurin-9-yl). This was kept for 48 h at the ambient temperature with 8 mL Me3SiBr in 80 mL MeCN, the Me3Si-ester dissolved in 100 mL 0.4 M [Et3NH+]HCO3- (pH 7.5) and allowed to stand for 30 min, and the crude product purified on ion exchangers to give 2.8 g title compound II (B = 6-methylthiopurin-9-yl) as a Na salt. The latter at 10-7% completely prevented reproduction of Pyrrhocoris apterus.

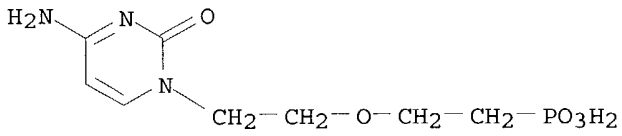
IT **138277-11-9DP**, trimethylsilyl derivs.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of, in preparation of insect sterilants)
RN 138277-11-9 HCAPLUS
CN Phosphonic acid, [2-[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]ethyl]-, ethyl trimethylsilyl ester (9CI) (CA INDEX NAME)



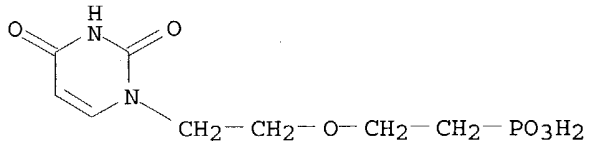
IT **138277-10-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with bromotrimethylsilane, in preparation of insect
sterilant)
RN 138277-10-8 HCAPLUS
CN Phosphonic acid, [2-[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]ethyl]-, monoethyl ester (9CI) (CA INDEX NAME)



IT **129431-98-7P 138277-05-1P 138277-06-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as insect sterilant)
RN 129431-98-7 HCAPLUS
CN Phosphonic acid, [2-[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]ethyl]- (9CI) (CA INDEX NAME)

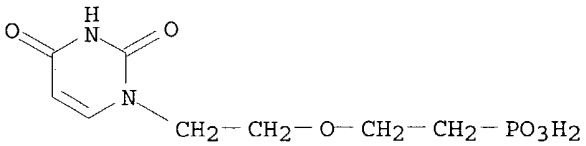


RN 138277-05-1 HCAPLUS
CN Phosphonic acid, [2-[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]ethyl]- (9CI) (CA INDEX NAME)



RN 138277-06-2 HCAPLUS
CN Phosphonic acid, [2-[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]ethyl]-, lithium salt (9CI) (CA INDEX NAME)

Searched by P. Ruppel



●x Li

L71 ANSWER 28 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:608461 HCAPLUS
DOCUMENT NUMBER: 115:208461
TITLE: Preparation of phosphorus-containing nucleoside analogs as antitumors and antivirals
INVENTOR(S): Kim, Choung Un; Martin, John C.; Misco, Peter F.; Luh, Bing Yu
PATENT ASSIGNEE(S): Bristol-Myers Co., USA
SOURCE: Eur. Pat. Appl., 48 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 398231	A2	19901122	EP 1990-109066	19900514
EP 398231	A3	19930602		
EP 398231	B1	19970716		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2015671	AA	19901115	CA 1990-2015671	19900427
CA 2015671	C	20000425		
ZA 9003647	A	19910130	ZA 1990-3647	19900514
AU 630953	B2	19921112	AU 1990-55012	19900514
AU 9055012	A1	19901115		
AT 155480	E	19970815	AT 1990-109066	19900514
ES 2104570	T3	19971016	ES 1990-109066	19900514
JP 03005493	A2	19910111	JP 1990-123262	19900515
JP 2900064	B2	19990602		
AU 9224592	A1	19921119	AU 1992-24592	19920918
AU 646594	B2	19940224		
US 5688778	A	19971118	US 1995-391312	19950217
US 5686611	A	19971111	US 1995-488339	19950607
US 5693798	A	19971202	US 1995-488337	19950607
US 5696265	A	19971209	US 1995-488340	19950607
US 5726174	A	19980310	US 1995-488338	19950607
US 5837871	A	19981117	US 1995-486991	19950607

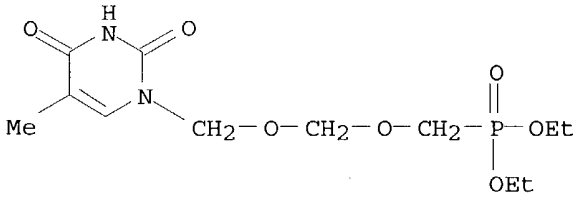
PRIORITY APPLN. INFO.:
US 1989-352303 A 19890515
US 1990-481569 A 19900222
US 1990-481659 19900222
US 1991-765774 B1 19910926
US 1995-391312 A3 19950217

OTHER SOURCE(S): MARPAT 115:208461
GI For diagram(s), see printed CA Issue.

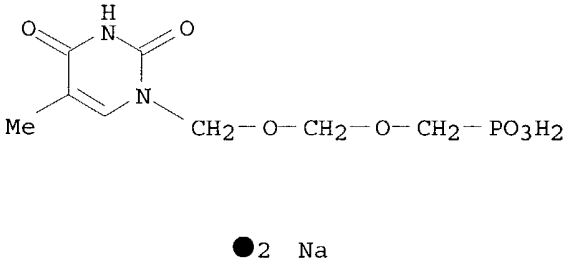
AB Title compds. XO-P(O)(OX1)CHROCHR1B [I; X, X1 = H, alkyl, cation; R, R1 = H, alkyl, hydroxyalkyl, alkanoyl; B = purinyl, pyrimidinyl], II [Y, Z = H, OH, (substituted) alkyl, or YZ = O, CH2], III [R2 = OH], IV, and their pharmaceutically acceptable salts, especially useful as retrovirus inhibitors, were prepared BzOCH2OCH2OBz [prepared from BzONa and (ClCH2)2O], was treated with 1-(trimethylsilyl)thymine (prepared from thymine and Me3SiCl) in CF3SO3SiMe3 at 25° for 8 h to give 1-[[(benzoyloxy)methoxy]methyl]thymine, which was condensed with (EtO)2P(O)CH2OH in benzene at 85° for 20 min to give I (X = X1 = Et, R = R1 = H, B = 1-thyminyl). 9-[3-(Phosphonomethoxy)methoxymethyl]guanine di-Na salt (preparation given) had an ID50 of 2.6 μg/mL against herpes simplex virus-1 compared with 0.5 μg/mL for acyclovir.

IT **131853-08-2P 134361-15-2P 134361-17-4P 134361-19-6P 136711-59-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antiviral and antitumor)

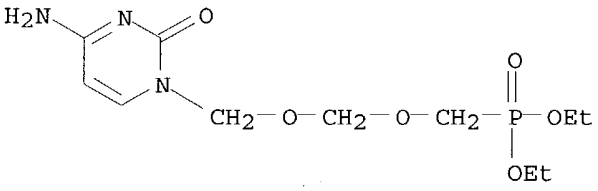
RN 131853-08-2 HCAPLUS
CN Phosphonic acid, [[[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 134361-15-2 HCAPLUS
CN Phosphonic acid, [[[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)

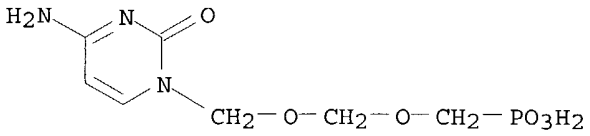


RN 134361-17-4 HCAPLUS
CN Phosphonic acid, [[[(4-amino-2-oxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



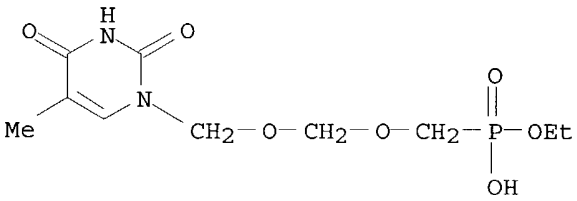
Searched by P. Ruppel

RN 134361-19-6 HCAPLUS
CN Phosphonic acid, [[[(4-amino-2-oxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)



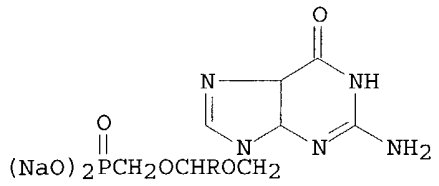
● 2 Na

RN 136711-59-6 HCAPLUS
CN Phosphonic acid, [[[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, monoethyl ester, monosodium salt (9CI) (CA INDEX NAME)

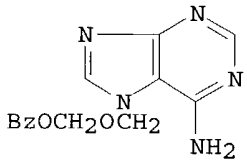


● Na

L71 ANSWER 29 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:450185 HCAPLUS
DOCUMENT NUMBER: 115:50185
TITLE: A new class of acyclic phosphonate nucleotide analogs: Phosphonate isosteres of acyclovir and ganciclovir monophosphates as antiviral agents
AUTHOR(S): Kim, Choung Un; Misco, Peter F.; Luh, Bing Yu; Hitchcock, Michael J. M.; Ghazzouli, Ismail; Martin, John C.
CORPORATE SOURCE: Pharm. Res. Inst., Bristol-Myers Squibb Co., Wallingford, CT, 06492, USA
SOURCE: Journal of Medicinal Chemistry (1991), 34(7), 2286-94
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 115:50185
GI



I



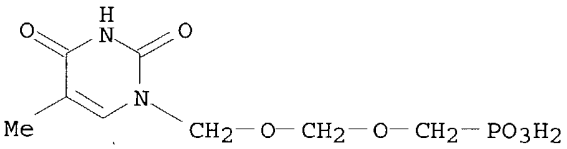
II

AB Novel phosphonate isosteres of acyclovir (ACV) and ganciclovir (DHPG) monophosphates I (R = H, CH2OH) were found to be potent and selective antiherpesvirus agents. In the series of phosphonate analogs of ACV monophosphate, only the guanine analog I (R = H) exhibited activity against herpesviruses, similar to the structure-activity relationship observed for base modification of ACV analogs. The phosphonate isostere of ACV monophosphate I (R = H) was more effective than ACV in the HSV-1 infected mouse model. The 3'-carba analog of 9-[3-hydroxy-2-(phosphonomethoxy)propyl]purines/ pyrimidines (adenine:HPMPA; guanine:HPMPG; cytosine:HPMPC) are devoid of antiherpesvirus activity. This result confirms that the β-oxygen atom of the phosphonomethyl ether functionality in HPMP-purines/pyrimidines plays a critical role for activity against herpesviruses. The crystal structure of [(benzoyloxy)methoxy]methyladenine II was determined

IT **134361-15-2P 134361-19-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiviral activity of)

RN 134361-15-2 HCAPLUS

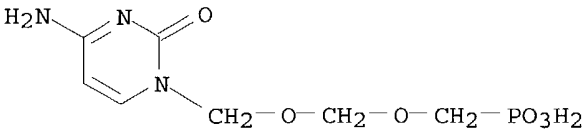
CN Phosphonic acid, [[[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

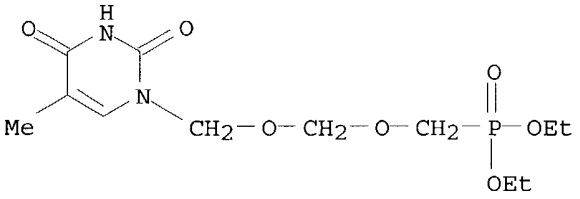
RN 134361-19-6 HCAPLUS

CN Phosphonic acid, [[[(4-amino-2-oxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)

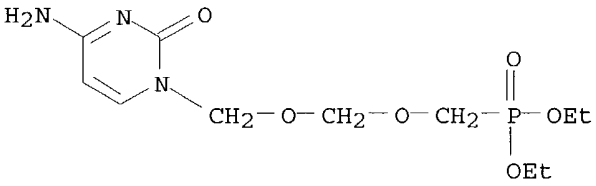


●2 Na

IT **131853-08-2P 134361-17-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)
RN 131853-08-2 HCAPLUS
CN Phosphonic acid, [[[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



RN 134361-17-4 HCAPLUS
CN Phosphonic acid, [[[(4-amino-2-oxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L71 ANSWER 30 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:409055 HCAPLUS
DOCUMENT NUMBER: 115:9055
TITLE: Preparation of diethyl (2-p-toluenesulfonyloxyethoxy)methanephosphonate as a virucide intermediate
INVENTOR(S): Holy, Antonin; Rosenberg, Ivan
PATENT ASSIGNEE(S): Czech.
SOURCE: Czech., 5 pp.
CODEN: CZXXA9
DOCUMENT TYPE: Patent
LANGUAGE: Czech
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

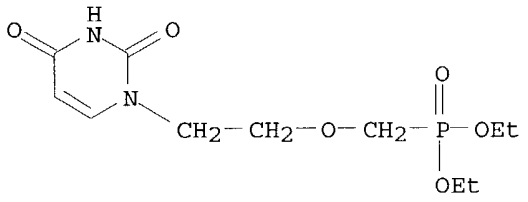
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CS 267590	B1	19900212	CS 1987-1527	19870306

PRIORITY APPLN. INFO.: CS 1987-1527 19870306
OTHER SOURCE(S): CASREACT 115:9055

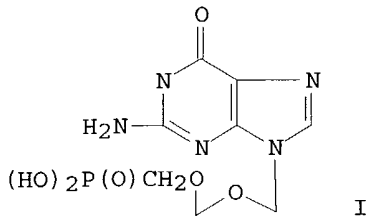
AB (EtO)2P(O)CH2OCH2CH2OSO2C6H4Me-p (I), useful for preparation of purine and pyrimidine derivs. (EtO)2P(O)CH2OCH2CH2B (B = purin-9-yl, pyrimidin-1-yl) as intermediates for virucidal N-(2-phosphonylmethoxyethyl)purines and -pyrimidines, was prepared by esterification of the phosphonylmethoxyethanol (EtO)2P(O)CH2OCH2CH2OH (II) with 1.1-1.2 equiv p-tosyl chloride in pyridine or CH2Cl2, in the presence of 1 equiv Et3N (based on tosyl chloride) at 0-30°. Thus, a mixture of 113.5 g II [preparation by deacetylation of 137.3 g (EtO)2P(O)CH2OCH2CH2OAc with a cation exchange resin given] and 88.4 mL Et3N in 250 mL CH2Cl2 was treated dropwise over 30 min by 121.5 g p-tosyl chloride in 250 mL CH2Cl2, the whole was stirred 2 h, 611 mg 4-dimethylaminopyridine was added, and stirring continued for 4 h to give 145.0 g I. The latter was used to prepare 9-(2-diethoxyphosphonylmethoxyethyl)adenine (58%), 2-amino-9-(2-diethoxyphosphonylmethoxyethyl)adenine (66%), and 1-(2-diethoxyphosphonylmethoxyethyl)uracil (42%).

IT **126354-53-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 126354-53-8 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



L71 ANSWER 31 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1991:82404 HCAPLUS
DOCUMENT NUMBER: 114:82404
TITLE: Synthesis of a phosphonate isostere of acyclovir monophosphate: a herpes virus active phosphonate nucleotide analog
AUTHOR(S): Kim, Choung Un; Misco, Peter F.; Luh, Bing Y.; Martin, John C.
CORPORATE SOURCE: Pharm. Res. Dev. Div., Bristol-Myers Squibb Co., Wallingford, CT, 06492-7660, USA
SOURCE: Heterocycles (1990), 31(9), 1571-4
CODEN: HTCYAM; ISSN: 0385-5414
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:82404
GI



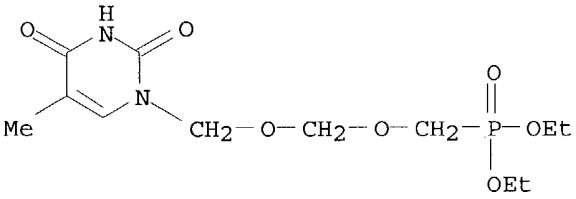
I

AB The title compound I was prepared by reaction of 2-amino-6-chloropurine Na salt with (EtO)2P(O)(CH2O)2CH2Cl, followed by saponification I had an ED50 against herpes simplex type 1 of 2.6 μg/mL.

IT **131853-08-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ester hydrolysis of)

RN 131853-08-2 HCAPLUS

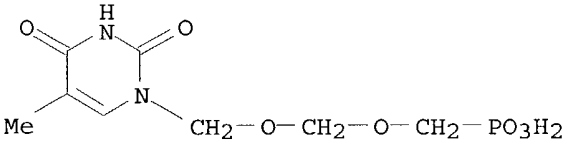
CN Phosphonic acid, [[[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)



IT **131853-09-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 131853-09-3 HCAPLUS

CN Phosphonic acid, [[[(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)methoxy]methoxy]methyl]- (9CI) (CA INDEX NAME)



L71 ANSWER 32 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1991:35417 HCAPLUS

DOCUMENT NUMBER: 114:35417

TITLE: Inhibition of avian myeloblastosis virus reverse transcriptase by diphosphates of acyclic phosphonylmethyl nucleotide analogs

AUTHOR(S): Votruba, Ivan; Travnicek, Miloslav; Rosenberg, Ivan; Otmar, Miroslav; Merta, Ales; Hrebabecky, Hubert; Holy, Antonin

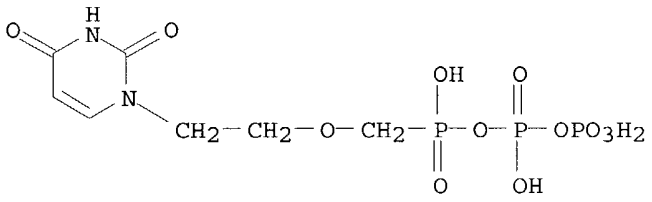
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czech Acad. Sci., Prague, 16610, Czech.

SOURCE: Antiviral Research (1990), 13(6), 287-93
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English

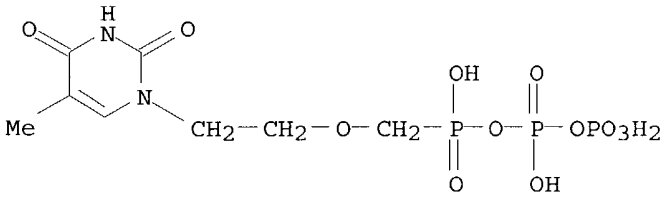
AB Diphosphates of N-(2-phosphonylmethoxyethyl) derivs. of heterocyclic nucleotide bases were studied in the endogenous oligo(dT)12-18 primed reaction of reverse transcriptase obtained from detergent-disrupted avian myeloblastosis virus retrovirions. These diphosphates (analogs of nucleotide 5'-triphosphates) exhibited an inhibitory activity towards reverse transcriptase. This inhibitory activity was dependent on the character of the heterocyclic base and decreased in the order: 2-aminoadenine > adenine > guanine >> cytosine >> thymine > uracil. The 2-aminoadenine derivative was more potent than either AZT-TP or ddTTP, while phosphonylmethoxyethyladenine had approx. the same potency as the two reference compds. (IC50 ≈ 1 μM AT 20 μM competing substrate). This finding is consistent with the antiviral activity of the parent nucleotide analogs against retroviruses (including HIV).

IT **130029-14-0 130029-16-2 130029-17-3**
RL: BIOL (Biological study)
(reverse transcriptase inhibition by, in avian myeloblastosis virus)

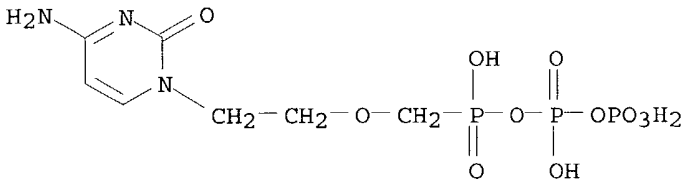
RN 130029-14-0 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)



RN 130029-16-2 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)



RN 130029-17-3 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)

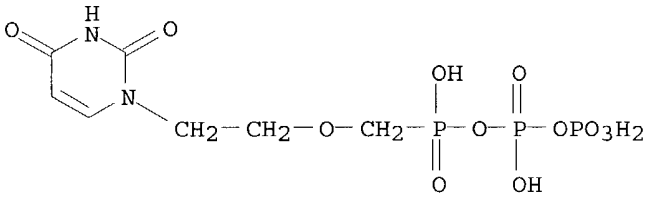


L71 ANSWER 33 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:624152 HCAPLUS
DOCUMENT NUMBER: 113:224152
TITLE: Inhibition of herpes simplex virus DNA polymerase by diphosphates of acyclic phosphonylmethoxyalkyl nucleotide analogs
AUTHOR(S): Merta, Ales; Votruba, Ivan; Rosenberg, Ivan; Otmar, Miroslav; Hrebabecky, Hubert; Holy, Antonin
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.
SOURCE: Antiviral Research (1990), 13(5), 209-18
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English

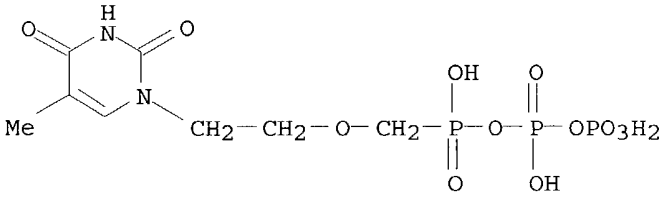
AB The inhibition of HSV-1 DNA polymerase and HeLa DNA polymerases α and β by diphosphoryl derivs. of acyclic phosphonylmethoxyalkyl nucleotide analogs was studied and compared with the inhibition by ACV-TP, araCTP, ddTTP, and AZT-TP. In the series of phosphonylmethoxyethyl (PME-) derivs. of heterocyclic bases, the inhibitory effect of their diphosphates on HSV-1 DNA polymerase decreased in the order 2-amino-PMEApp (Ki = 0.03 μM) » PMEGpp > PMEApp > PMETpp » PMECpp » n8z7PMEApp > PMEUpp. The diphosphate derivative of the antiherpes agent (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenine (HPMPA) proved to be a relatively weak inhibitor of HSV-1 DNA polymerase (Ki = 1.4 μM). The inhibitors could be divided into three groups: (a) the diphosphoryl derivs. of acyclic nucleotide analogs (PME-type and HPMPA) and ACV-TP specifically inhibit HSV-1 DNA polymerase and DNA polymerase α and do not inhibit DNA polymerase β; (b) AZT-TP and ddTTP are effective only against DNA polymerase β, and (c) araCTP inhibits all three enzymes. When dATP was omitted from the reaction mixture, the addition of HPMPApp stimulated DNA synthesis by HSV-1 DNA polymerase indicating that HPMPApp is an alternative substrate for in vitro DNA synthesis catalyzed by this enzyme.

IT **130029-14-0 130029-16-2 130029-17-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral activity of, against herpes simplex virus, DNA polymerase inhibition in)

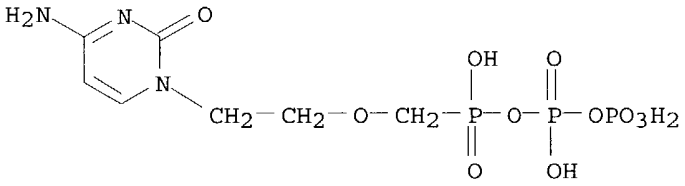
RN 130029-14-0 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)



RN 130029-16-2 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)



RN 130029-17-3 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)

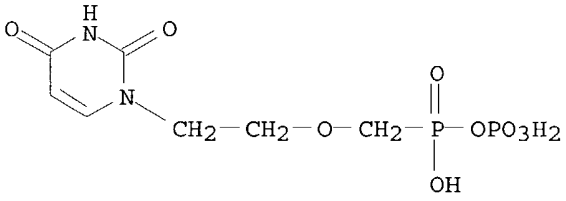


L71 ANSWER 34 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:584251 HCAPLUS
DOCUMENT NUMBER: 113:184251
TITLE: Phosphonylmethyl ethers of acyclic nucleoside analogs: inhibitors of HSV-1 induced ribonucleotide reductase
AUTHOR(S): Cerny, Jaroslav; Votruba, Ivan; Vonka, Vladimir; Rosenberg, Ivan; Otmar, Miroslav; Holy, Antonin
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 16610/6, Czech.
SOURCE: Antiviral Research (1990), 13(5), 253-63
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Diphosphates of N-(S)-(3-hydroxy-2-phosphonylmethoxypropyl) (HPMP) and N-(2-phosphonylmethoxyethyl) (PME) derivs. of purine and pyrimidine heterocyclic bases inhibit HSV-1 encoded ribonucleotide reductase. Of the compds. studied, the most efficient inhibitors of CDP reduction (at 5.1 μmol/L) by the HSV-1-encoded enzyme are HPMPApp (IC50 = 0.9 μmol/L) and PMEApp (IC50 = 8 μmol/L). PMEApp does not inhibit the enzyme isolated from the mutant HSV-1 KOS strain which is resistant to PMEA at a concentration of 100 μg/mL. The enzyme isolated from the PMEA-resistant virus

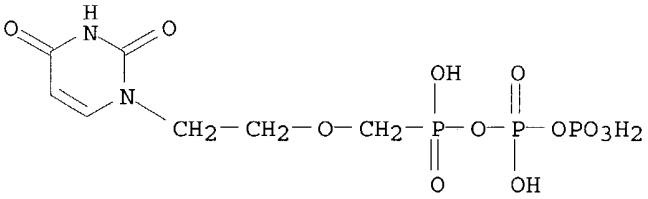
strain is also sensitive to inhibitory effects of hydroxyurea and HPMPApp. Thus, the inhibitory potency of HPMPApp and PMEApp toward HSV-1 encoded ribonucleotide reductase might be connected with the anti-HSV activity of HPMPA and PMEA.

IT **130029-13-9 130029-14-0 130029-15-1 130029-16-2 130029-17-3 130042-69-2**
RL: BIOL (Biological study)
(HSV1-induced ribonucleotide reductase inhibition by)

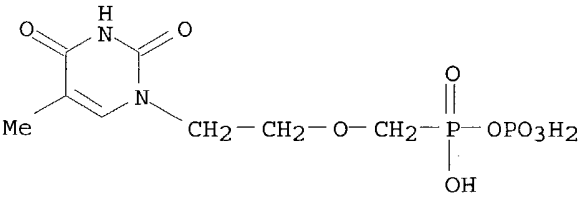
RN 130029-13-9 HCAPLUS
CN Isohypophosphoric acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



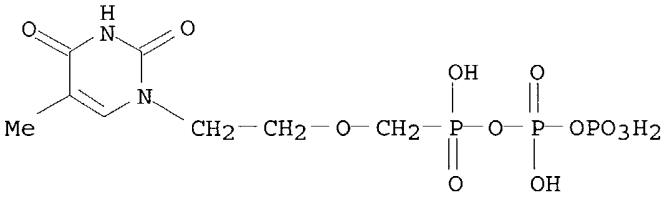
RN 130029-14-0 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)



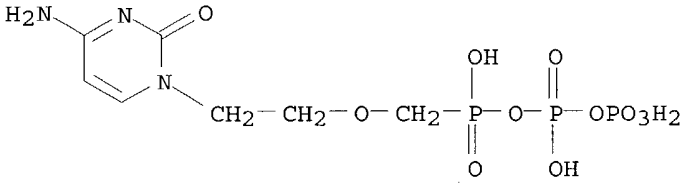
RN 130029-15-1 HCAPLUS
CN Isohypophosphoric acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



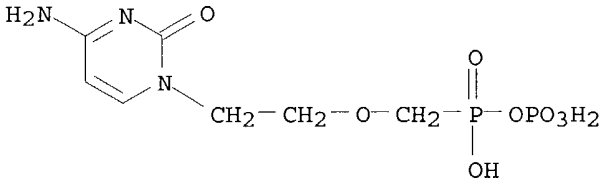
RN 130029-16-2 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)



RN 130029-17-3 HCAPLUS
CN Diphosphoric acid, monoanhydride with [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]phosphonic acid (9CI) (CA INDEX NAME)

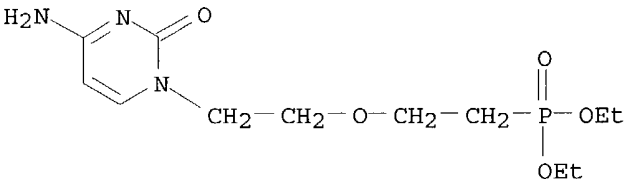


RN 130042-69-2 HCAPLUS
CN Isohypophosphoric acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

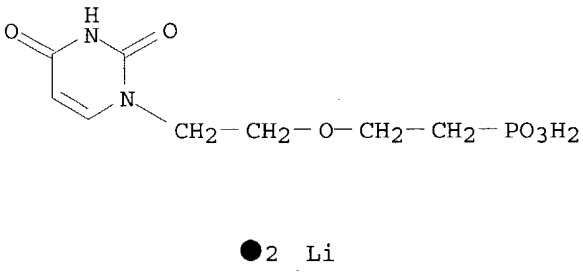


L71 ANSWER 35 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:532671 HCAPLUS
DOCUMENT NUMBER: 113:132671
TITLE: Acyclic nucleotide analogs. VIII. Synthesis of N-(2-(2-phosphonylethoxy)ethyl) derivatives of heterocyclic bases
AUTHOR(S): Holy, Antonin; Rosenberg, Ivan; Dvorakova, Hana
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications (1990), 55(3), 809-18
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Reaction of bis(2-chloroethyl) ether with (EtO)3P afforded di-Et 2-chloroethoxyethylphosphonate. This compound reacts with Na salts of heterocyclic bases to give di-Et esters of N-[2-(2-phosphonylethoxy)ethyl] derivs. of purine and pyrimidine bases. These compds. on reaction with Me3SiBr and subsequent hydrolysis were converted into N-[2-(phosphonylethoxy)ethyl] derivs., BCH2CH2OCH2CH2P(O)(OH)2 (B = purine or pyrimidine base).

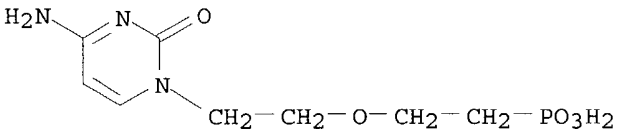
IT **129432-05-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and silylation and hydrolysis of)
RN 129432-05-9 HCAPLUS
CN Phosphonic acid, [2-[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]ethyl]-, diethyl ester (9CI) (CA INDEX NAME)



IT **129220-97-9P 129431-98-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 129220-97-9 HCAPLUS
CN Phosphonic acid, [2-[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]ethyl]-, dilithium salt (9CI) (CA INDEX NAME)



RN 129431-98-7 HCAPLUS
CN Phosphonic acid, [2-[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]ethyl]- (9CI) (CA INDEX NAME)



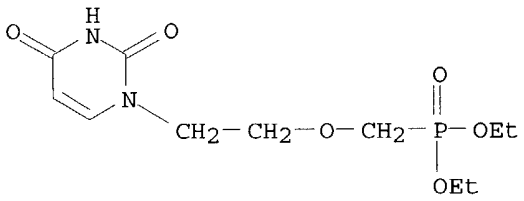
L71 ANSWER 36 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1990:179685 HCAPLUS
DOCUMENT NUMBER: 112:179685
TITLE: Synthesis of N-(2-phosphonylmethoxyethyl) derivatives of heterocyclic bases
AUTHOR(S): Holy, Antonin; Rosenberg, Ivan; Dvorakova, Hana
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, 166 10, Czech.
SOURCE: Collection of Czechoslovak Chemical Communications

(1989), 54(8), 2190-210
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 112:179685

AB The preparation of N-(2-phosphonylmethoxyethyl) derivs. of purine and pyrimidine bases, B-CH2CH2OCH2P(O)(OH)2 (I; B = pyrimidin-1-yl, pyrin-9-yl), as analogs of the antiviral 9-(2-phosphonylmethoxyethyl)adenine, is described. The synthesis consists of alkylation of alkali metal salts of heterocyclic bases or their N- or O-substituted derivs. with XCH2CH2OCH2P(O)(OEt)2 (X = tosyloxy, Cl, Br). The obtained N-(2-diethoxyphosphonylmethoxyethyl) derivs. of heterocyclic bases were treated with bromotrimethylsilane to give I. I were prepared from pyrimidines (uracil, cytosine and their 5-Me derivs.), purines (adenine and its N6- and C(2)-substituted derivs., hypoxanthine, guanine, 6-hydrazinopurine and 6-methylthiopurine etc.) and their analogs (3-deazaadenine etc.). Some I showed significant antiviral activity against DNA viruses and retroviruses.

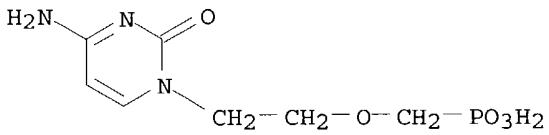
IT **126354-53-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and conversion of, to (phosphonylmethoxyethyl)uracil)

RN 126354-53-8 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)

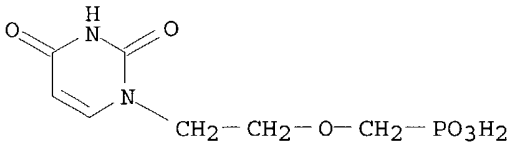


IT **117087-39-5P 126354-54-9P 126354-58-3P**
126354-60-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)

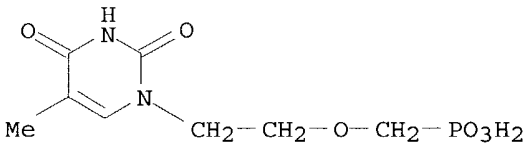


RN 126354-54-9 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, dilithium salt (9CI) (CA INDEX NAME)



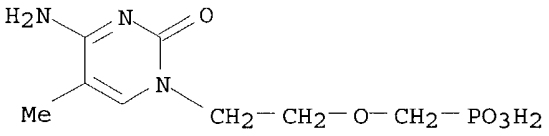
●2 Li

RN 126354-58-3 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, dilithium salt (9CI) (CA INDEX NAME)



●2 Li

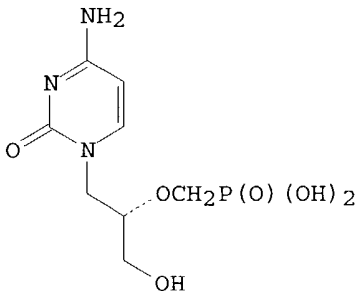
RN 126354-60-7 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-5-methyl-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, disodium salt (9CI) (CA INDEX NAME)



●2 Na

L71 ANSWER 37 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:423886 HCAPLUS
DOCUMENT NUMBER: 111:23886
TITLE: Synthesis and antiviral activity of the nucleotide analog (S)-1-[3-hydroxy-2-(phosphonylmethoxy)propyl]cystosine
AUTHOR(S): Bronson, Joanne J.; Ghazzouli, Ismail; Hitchcock, Michael J. M.; Webb, Robert R., II; Martin, John C.
CORPORATE SOURCE: Pharm. Res. Dev. Div., Bristol-Myers, Wallingford, CT, 06492-7660, USA
SOURCE: Journal of Medicinal Chemistry (1989), 32(7), 1457-63
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:23886
GI

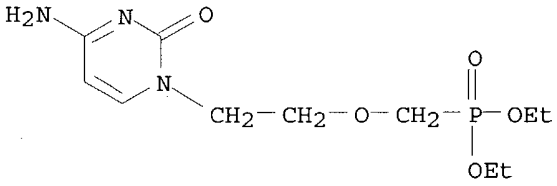


I

AB The title compound I was prepared on a multigram scale in 18% overall yield from (R)-2,3-O-isopropylideneglycerol. The key step in the nine-step synthetic route is coupling of cytosine with (R)-PhCH2OCH2CH[OCH2P(O)(OL)2]CH2O3SMe. I has good activity against herpes simplex virus types 1 and 2 in vitro, although it was 10-fold less potent than acyclovir (II). I exhibited greater activity than II against a thymidine kinase-deficient strain of HSV 1 and was more potent than ganciclovir against human cytomegalovirus. In vivo, I showed exceptional potency against HSV 1 systemic infection in mice, having an ED50 of 0.1 mg/kg per day (i.p.) compared with 50 mg/kg per day for II. I was also more efficacious than II in the topical treatment of HSV 1 cutaneous lesions in guinea pigs.

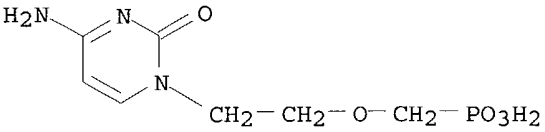
IT **120362-31-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and ester hydrolysis of)

RN 120362-31-4 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]-, diethyl ester (9CI) (CA INDEX NAME)

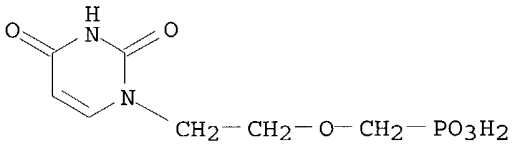


IT **117087-39-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and virucidal activity of)

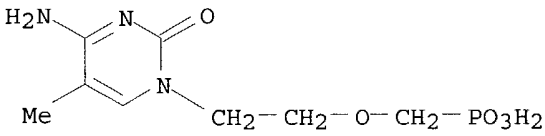
RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



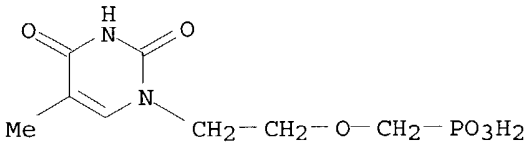
L71 ANSWER 38 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:423866 HCAPLUS
DOCUMENT NUMBER: 111:23866
TITLE: Synthesis and evaluation of acyclic nucleotide analogs
AUTHOR(S): Holy, Antonin; Rosenberg, Ivan; Dvorakova, Hana; DeClercq, Erik
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Czech. Acad. Sci., Prague, Czech.
SOURCE: Nucleosides & Nucleotides (1988), 7(5-6), 667-70
CODEN: NUNUD5; ISSN: 0732-8311
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 111:23866
AB Acyclic nucleotide analogs derived from antiviral 9-(2-phosphonylmethoxyethyl)adenine by modification at the side chain or by alternation of the heterocyclic base were synthesized and investigated for their antiviral activity.
IT **113852-43-0P 113852-44-1P 116455-16-4P 117087-39-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antiviral activity of)
RN 113852-43-0 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



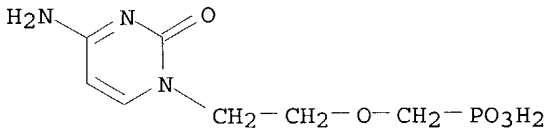
RN 113852-44-1 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-5-methyl-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 116455-16-4 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



L71 ANSWER 39 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:75170 HCAPLUS
DOCUMENT NUMBER: 110:75170
TITLE: Preparation and testing of N-phosphonylmethoxyalkyl derivatives of pyrimidine and purine bases with antiviral activity
INVENTOR(S): Holy, Antonin; Rosenberg, Ivan; De Clercq, Erik
PATENT ASSIGNEE(S): Ceskoslovenska Akademie Ved, Czech.; Rega Foundation
SOURCE: Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 253412	A2	19880120	EP 1987-110399	19870717
EP 253412	A3	19890426		
EP 253412	B1	19901031		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CS 264222	B1	19890613	CS 1986-5469	19860718
DK 8703734	A	19880119	DK 1987-3734	19870717
DK 170646	B1	19951120		
FI 8703165	A	19880119	FI 1987-3165	19870717
FI 86856	B	19920715		
FI 86856	C	19921026		
AU 8775759	A1	19880121	AU 1987-75759	19870717
AU 600002	B2	19900802		
ZA 8705283	A	19880330	ZA 1987-5283	19870717
AT 57932	E	19901115	AT 1987-110399	19870717
US 5142051	A	19920825	US 1987-74900	19870717
IL 83235	A1	19921115	IL 1987-83235	19870717
ES 2036194	T3	19930516	ES 1987-110399	19870717
JP 63045289	A2	19880226	JP 1987-179877	19870718
JP 08022866	B4	19960306		
US 5641763	A	19970624	US 1994-320591	19941011
US 5869467	A	19990209	US 1995-412398	19950328

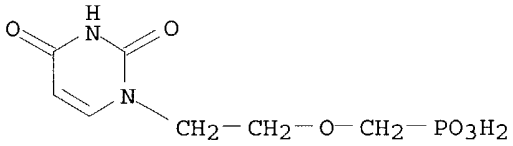
PRIORITY APPLN. INFO.: CS 1986-5469 19860718

EP 1987-110399 19870717
US 1987-74900 19870717
US 1992-891701 19920601
US 1994-320591 19941011

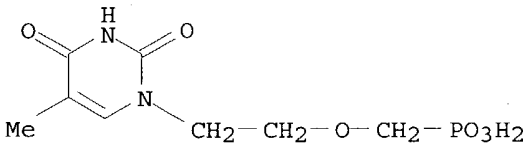
AB BCH2CHROCH2P(:O)(OH)2 (I) [R = H, CH2OH; B = (substituted) pyrimidin-1-yl, pyrimidin-3-yl, purin-3-yl, purin-7-yl, purin-9-yl, excluding adenin-9-yl], useful as virucides, were prepared Isoamyl nitrite was added to 9-(2-phosphonylmethoxyethyl)adenine in HOAc and the mixture was allowed to stand 72 h at room temperature to give 9-(2-phosphonylmethoxyethyl)hypoxanthi ne. I had IC50's of 7-150 μg/mL against HSV-1, vs 0.02 μg/mL for 5-(2-bromovinyl)-2'-deoxyuridine.

IT **113852-43-0P 116455-16-4P 117087-39-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as virucide)

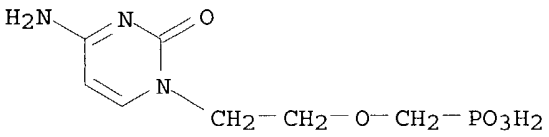
RN 113852-43-0 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 116455-16-4 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



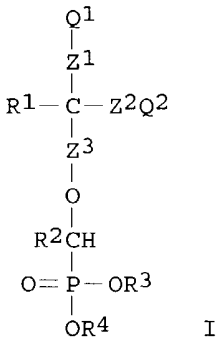
L71 ANSWER 40 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:590136 HCAPLUS
DOCUMENT NUMBER: 109:190136
TITLE: Antiviral phosphonomethoxyalkylpurines and -pyrimidines and their preparation.
INVENTOR(S): Webb, Robert R., II; Bronson, Joanne J.; Martin, John

C.
PATENT ASSIGNEE(S): Bristol-Myers Co., USA
SOURCE: Eur. Pat. Appl., 73 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 269947	A1	19880608	EP 1987-116996	19871117
EP 269947	B1	19920722		
EP 269947	B2	19961016		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AU 8781250	A1	19880519	AU 1987-81250	19871116
AU 613592	B2	19910808		
IL 84477	A1	19951208	IL 1987-84477	19871116
DK 8706040	A	19880519	DK 1987-6040	19871117
JP 63170388	A2	19880714	JP 1987-290469	19871117
ZA 8708607	A	19880727	ZA 1987-8607	19871117
AT 78485	E	19920815	AT 1987-116996	19871117
ES 2033774	T3	19930401	ES 1987-116996	19871117
CA 1339780	A1	19980324	CA 1987-551979	19871117
US 5650510	A	19970722	US 1992-829784	19920131
US 5854228	A	19981229	US 1995-473826	19950607

PRIORITY APPLN. INFO.:
US 1986-932112 19861118
US 1987-114340 19871104
EP 1987-116996 19871117
US 1988-249809 19880927
US 1992-829784 19920131

OTHER SOURCE(S): MARPAT 109:190136
GI

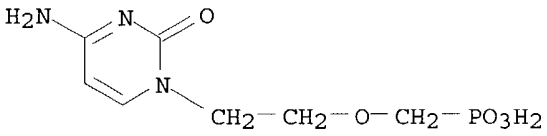


I

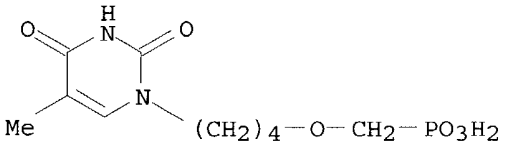
AB The title compds. I (Q1 = purine or pyrimidine base selected from adenine, xanthine, hypoxanthine, guanine, 8-bromoguanine, 8-hydroxyguanine, 8-methylguanine, cytosine, uracil, etc.; Z1-Z3 = bond, C1-4 alkylene, with the proviso that when Q1 is adenine and Z1 is methylene, Z2 cannot be a chemical bond; Q2 = H, OH with the proviso that when Q1 is adenine and Q2 is H, Z1 can only be C4H8; R1, R2 = H, C1-4 alkyl; R3, R4 = H, C1-6 alkyl, phenyl, and phenylalkylene), useful as antivirals, were prepared Reaction of N2-acetylguanine with 2-(diethylphosphonomethoxy)-1-iodoethane,

followed by hydrolysis in aqueous MeNH2, treatment with Me3SiBr, and workup, gave 9-(2-(phosphonomethoxy)ethyl)guanine, which in vitro exhibited an ID50 of <0.6 μg/mL vs. herpes simplex type 1, vs. an ID50 of 0.5 μg/mL for acyclovir.

IT **117087-39-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antiviral agent)
RN 117087-39-5 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



IT **117087-02-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as antiviral agent)
RN 117087-02-2 HCAPLUS
CN Phosphonic acid, [[4-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)butoxy]methyl]- (9CI) (CA INDEX NAME)

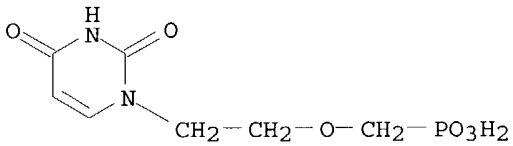


L71 ANSWER 41 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:542024 HCAPLUS
DOCUMENT NUMBER: 109:142024
TITLE: Phosphonylmethoxyethyl purine derivatives, a new class of anti-human immunodeficiency virus agents
AUTHOR(S): Pauwels, Rudi; Balzarini, Jan; Schols, Dominique; Baba, Masanori; Desmyter, Jan; Rosenberg, Ivan; Holy, Antonin; De Clercq, Erik
CORPORATE SOURCE: Rega Inst. Med. Res., Kathol. Univ. Leuven, Louvain, B-3000, Belg.
SOURCE: Antimicrobial Agents and Chemotherapy (1988), 32(7), 1025-30
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A study of the structure-activity relationship of a series of newly synthesized phosphonylmethoxyalkyl purine and pyrimidine derivs. revealed that several adenine derivs. substituted at the N9 position by a 2-phosphonylmethoxyethyl (PME) group inhibited human immunodeficiency virus (HIV)-induced cytopathogenicity and HIV antigen expression in vitro at concns. significantly below the toxicity threshold for the host cells.

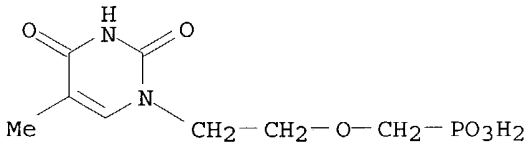
In terms of anti-HIV potency in MT-4 cells, the PME 2,6-diaminopurine derivative (50% ED [ED50], 1 μM) ranked first, followed by the PME adenine derivative (ED50, 2 μM [MT-4]) and the PME 2-monoaminopurine derivative (ED50, 45 μM). Antiretroviral activity was also demonstrated in ATH8 and H9 cells, which were de novo infected with HIV, and extended to C3H mouse fibroblasts infected with Maloney murine sarcoma virus. Unlike 2',3'-dideoxyadenosine, these compds. were not degraded by deaminases derived from bovine intestine.

IT **113852-43-0 116455-16-4**
RL: BIOL (Biological study)
(human immunodeficiency virus inhibition by)

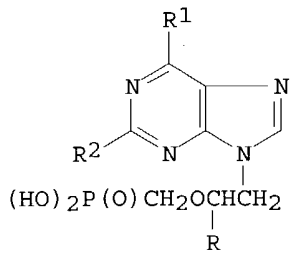
RN 113852-43-0 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



RN 116455-16-4 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-5-methyl-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



L71 ANSWER 42 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:160978 HCAPLUS
DOCUMENT NUMBER: 108:160978
TITLE: Phosphonylmethoxyalkylpurines and -pyrimidines as inhibitors of African swine fever virus replication in vitro
AUTHOR(S): Gil-Fernandez, Carmen; Garcia-Villalon, Dolores; De Clercq, Erik; Rosenberg, Ivan; Holy, Antonin
CORPORATE SOURCE: Cent. Invest. Biologicas, Consejo Super. Invest. Cientificas, Madrid, 28006, Spain
SOURCE: Antiviral Research (1987), 8(5-6), 273-81
CODEN: ARSRDR; ISSN: 0166-3542
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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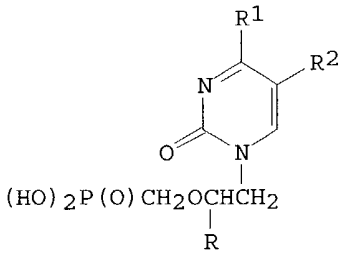
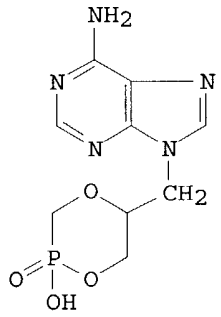


II

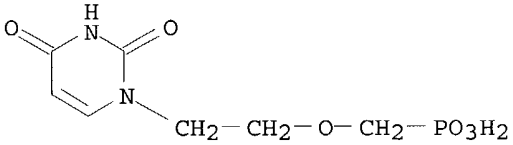


III

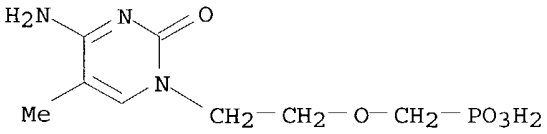
AB Several phosphonylmethoxyalkylpurine (I; R = H or CH2OH; R1 = H, OH, or NH2; R2 = H, NH2, or Me) and pyrimidine (II; R-R2 same as for I) derivs. related to (S)-9-(3-hydroxy-2-phosphonylmethoxypropyl)adenosine [(S)-HPMPA] and 9-(2-phosphonylmethoxyethyl)adenine were evaluated as inhibitors of African swine fever virus (ASFV) replication in Vero cells. (S)-HPMPA was previously shown to inhibit ASFV replication at a min. inhibitory concentration (MIC) of 0.01 μg/mL with a selectivity index of 1500. Of the new compds. tested, the following emerged as the most potent and selective inhibitors of ASFV replication: the cyclic phosphonate of (S)-HPMPA (III) with an MIC of 0.2 μg/mL and a selectivity index of 2500, the 2,6-diaminopurine analog of (S)-HPMPA with an MIC of 0.5 μg/mL and a selectivity index of 1400, and the cytosine and guanine analogs with an MIC of 1 μg/mL and a selectivity index of 600-700.

IT **113852-43-0 113852-44-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiviral activity of, African swine fever virus inhibition in)

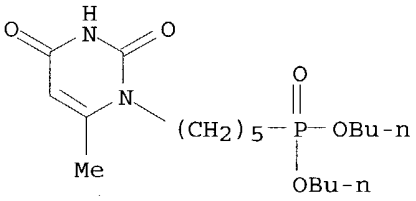
RN 113852-43-0 HCAPLUS
CN Phosphonic acid, [[2-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



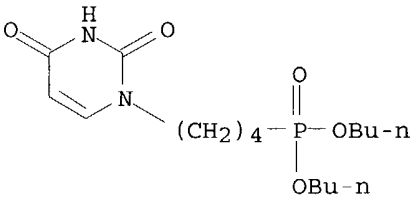
RN 113852-44-1 HCAPLUS
CN Phosphonic acid, [[2-(4-amino-5-methyl-2-oxo-1(2H)-pyrimidinyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)



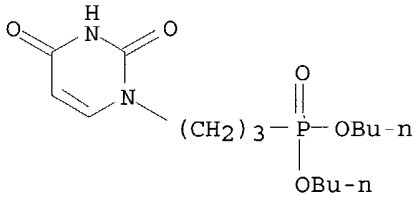
L71 ANSWER 43 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1975:564327 HCAPLUS
DOCUMENT NUMBER: 83:164327
TITLE: Synthesis and properties of pyrimidinylalkylphosphonic acids. 9. Synthesis of certain ω-(oxodihydropyrimidin-N-yl)alkyl phosphates and ω-(oxodihydropyrimidin-N-yl)alkylphosphonates
AUTHOR(S): Reznik, V. S.; Shvetsov, Yu. S.; Bakulin, V. S.; Salikhov, I. Sh.
CORPORATE SOURCE: Inst. Org. Fiz. Khim. im. Arbuzova, Kazan, USSR
SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1975), (6), 1397-401
CODEN: IASKA6; ISSN: 0002-3353
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Pyrimidinedione phosphonates (I, R = P(O)(OEt)2, n = 4,5) were prepared in 79 and 70.5% yields by treating I (R = Cl, Br) with P(OEt)3. Treatment of II with ClP(O)(OPh)2 gave 80% III.
IT **56826-05-2P 56826-07-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 56826-05-2 HCAPLUS
CN Phosphonic acid, [5-(3,4-dihydro-6-methyl-2,4-dioxo-1(2H)-pyrimidinyl)pentyl]-, dibutyl ester (9CI) (CA INDEX NAME)



RN 56826-07-4 HCAPLUS
CN Phosphonic acid, [4-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)butyl]-, dibutyl ester (9CI) (CA INDEX NAME)

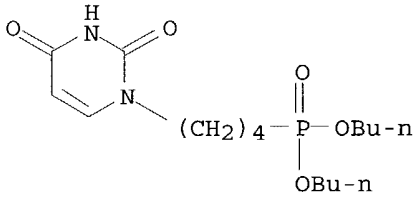


L71 ANSWER 44 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1975:564298 HCAPLUS
DOCUMENT NUMBER: 83:164298
TITLE: Synthesis and properties of pyrimidinylalkylphosphonic acids. 10. Chemical transformations of isomeric uracilphosphates
AUTHOR(S): Reznik, V. S.; Bakulin, V. S.; Shvetsov, Yu. S.; Ivanov, B. E.
CORPORATE SOURCE: Inst. Org. Fiz. Khim. im. Arbuzova, Kazan, USSR
SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1975), (6), 1401-5
CODEN: IASKA6; ISSN: 0002-3353
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Reaction of ClP(O)(OPh)2 with the pyrimidinedione salt I gave II (n = 3,4). Similarly reaction of ClP(O)(OPh)2 with III gave IV (R = PhCH2) and V (R = (CH2)3P(O)(OBu)2). Treatment of VI (R1 = OP(O)(OPh)2) with HCl gave VI.HCl (R1 = Cl).
IT **56825-95-7 56862-14-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with diphenyl phosphorochloridate)
RN 56825-95-7 HCAPLUS
CN Phosphonic acid, [3-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)propyl]-, dibutyl ester, sodium salt (9CI) (CA INDEX NAME)



● Na

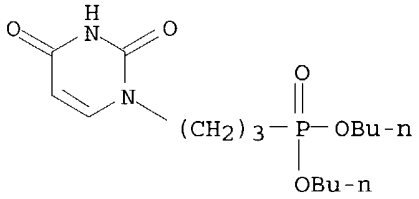
RN 56862-14-7 HCAPLUS
CN Phosphonic acid, [4-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)butyl]-, dibutyl ester, monosodium salt (9CI) (CA INDEX NAME)



● Na

L71 ANSWER 45 OF 45 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1973:453473 HCAPLUS
DOCUMENT NUMBER: 79:53473
TITLE: Synthesis and properties of pyrimidinylalkylphosphonic acids. 6. Reaction of some hydroxypyrimidines with dibutyl 3-chloropropyl phosphonate
AUTHOR(S): Reznik, V. S.; Bakulin, V. S.; Ivanov, B. E.
CORPORATE SOURCE: Inst. Org. Fiz. Khim. im. Arbuzova, Kazan, USSR
SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1973), (4), 875-8
CODEN: IASKA6; ISSN: 0002-3353
DOCUMENT TYPE: Journal
LANGUAGE: Russian
GI For diagram(s), see printed CA Issue.
AB Uracil Na salt reacted with Cl(CH2)3P(O(O3Bu)2 in hot BuOH or DMF to form mixed I [R = H (II), (CH2)3P(O)(OBu)2]. The Na salts of 2-amino-6-methyl-4-pyrimidinol and 6-methyluracil gave both N- and O-alkylation, not separable. Bromination of II gave the 2,4-dioxo-5-bromo-1,2,3,4-tetrahydropyrimidinyl analog as a structure proof.
IT **42078-22-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 42078-22-8 HCAPLUS
CN Phosphonic acid, [3-(3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)propyl]-, dibutyl ester (9CI) (CA INDEX NAME)



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